STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 144373

TO: Tamthom Troung
Location: rem/5b19/5c18
Art Unit: 1624
Tuesday, February 15, 2005
Case Serial Number: 09/806836

From: Paul Schulwitz
Location: Biotech-Chem Library
REM-1A65
Phone: (571)272-2527

paul.schulwitz@uspto.gov

Search Notes

Examiner Troung,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2527

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.

14373

Scientific and Technical Information Center

mg

Request a Search

Search requests relating to **published applications, patent families, and litigation** may be submitted by filling out this form and clicking on "Send."

For all other search requests, fill out the form, print, and submit the printout with any attachments to the STIC facility serving your Technology Center.

Tech Center:

(•) TC 1600 ( ) TC 1700 ( ) TC 2100 ( ) TC 2600 ( ) TC 2800
( ) TC2900 ( ) TC 3600 ( ) TC 3700 ( ) Law Lib ( ) Other

Enter your Contact Information below:

Name: TRUONG, TAMTHOM
Employee Number: 74142 Phone: X 20676
Art Unit or Office: 1624 Building & Room Number: REM 5C18

Enter the case serial number (Required): 09/806,836
If not related to a patent application, please enter NA here.

Class / Subclass(es) 514/266.2

Earliest Priority Filing Date: 10-8-99

Format preferred for results:
☐ *Paper* ☐ *Diskette* ☐ *E-mail*

Provide detailed information on your search topic:

- In your own words, describe in detail the concepts or subjects you want us to search.
- Include synonyms, keywords, and acronyms. Define terms that have special meanings.
- *For Chemical Structure Searches Only*
  Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers
- *For Sequence Searches Only*
  Include all pertinent information (parent, child, divisional, or issued patent numbers) along with

RECEIVED FEB - 7 2005 (STIC)

the appropriate serial number.
- *For Foreign Patent Family Searches Only*
  Include the country name and patent number.
- Provide examples or give us relevant citations, authors, etc., if known.
- FAX or send the **abstract, pertinent claims** (not all of the claims), **drawings, or chemical structures** to your EIC or branch library.

Enter your Search Topic Information below:

PLEASE SEARCH CLAIMS 11, 12, 13, 18 AND 19

Special Instructions and Other Comments:
(For fastest service, let us know the best times to contact you, in case the searcher needs further clarification on your search.)

Press ALT + F, then P to print this screen for your own information.

SEND RESET

2-(ethylpiperidin-4-yl)ethoxy, 3-(ethylpiperidin-3-yl)propoxy,
3-(ethylpiperidin-4-yl)propoxy, 2-((2-methoxyethyl)piperidin-3-yl)ethoxy,
2-((2-methoxyethyl)piperidin-4-yl)ethoxy, 3-((2-methoxyethyl)piperidin-3-yl)propoxy,
3-((2-methoxyethyl)piperidin-4-yl)propoxy,
2-((2-methylsulphonylethyl)piperidin-3-yl)ethoxy,
2-((2-methylsulphonylethyl)piperidin-4-yl)ethoxy,
3-((2-methylsulphonylethyl)piperidin-3-yl)propoxy,
3-((2-methylsulphonylethyl)piperidin-4-yl)propoxy, 1-isopropylpiperidin-2-ylmethyl,
1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl,
2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl,
2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl,
3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl,
3-(4-methylpiperazin-1-yl)propoxy, 1-methylpiperidin-4-ylmethoxy,
1-(2-methylsulphonylethyl)piperidin-4-ylmethoxy,
1-(2-pyrrolidinylethyl)piperidin-4-ylmethoxy,
1-(3-pyrrolidinylpropyl)piperidin-4-ylmethoxy, 1-(2-piperidinylethyl)piperidin-4-ylmethoxy,
1-(3-piperidinylpropyl)piperidin-4-ylmethoxy, 1-(2-morpholinoethyl)piperidin-4-ylmethoxy,
1-(3-morpholinopropyl)piperidin-4-ylmethoxy,
1-(2-thiomorpholinoethyl)piperidin-4-ylmethoxy,
1-(3-thiomorpholinopropyl)piperidin-4-ylmethoxy,
1-(2-azetidinylethyl)piperidin-4-ylmethoxy or 1-(3-azetidinylpropyl)piperidin-4-ylmethoxy.

Claim 11 (**previously presented**): A compound as claimed in claim 18 selected from:

4-~~(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy~~-7-(1-methylpiperidin-4-ylmethoxy)-~~quinazoline,~~ 264208-12-0

4-~~(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy~~-7-(3-(4-methylpiperazin-1-yl)-propoxy)quinazoline, 264208-18-6

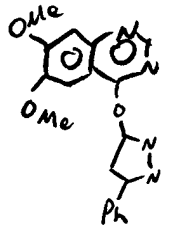
~~6-methoxy~~-7-~~(2-(2-methoxyethoxy)ethoxy)~~-4-~~(5-phenylpyrazol-3-yloxy)~~quinazoline, 264208-31-3

4-~~(5-(3-furyl)pyrazol-3-yloxy)-6-methoxy~~-7-(3-morpholinopropoxy)quinazoline, 264208-33-5

6-methoxy-7-(3-morpholinopropoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline, 264207-50-3
7-(2-(imidazol-1-yl)ethoxy)-6-methoxy-4-(5-phenylpyrazol-3-yloxy)quinazoline, 264208-35-7
4-(5-(4-chlorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline, 264207-72-9
6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)-4-(5-phenylpyrazol-3-yloxy)-quinazoline, 264207-76-3
6-methoxy-7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline, 264207-54-7
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(2-(1,2,3-triazol-1-yl)ethoxy)-quinazoline and 264208-14-2
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(1-(2-methylsulphonylethyl)-piperidin-4-ylmethoxy)quinazoline, 264208-16-4
and salts thereof.

Claim 12 (**previously presented**): A compound as claimed in claim 18 selected from:
7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline, 264208-38-0
4-(5-(2-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline, 264207-96-7
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(3-nitrophenyl)pyrazol-3-yloxy)quinazoline, 264207-98-9
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-nitrophenyl)pyrazol-3-yloxy)quinazoline, 264208-00-6
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-pyridyl)pyrazol-3-yloxy)quinazoline, 264207-74-1
4-(5-(4-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline, and 264208-41-5
6-methoxy-7-(2-methoxyethoxy)-4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)quinazoline, 264207-68-3
and salts thereof.

Claim 13 (**previously presented**): A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need of such treatment which comprises administering to such animal an effective amount of a compound selected from the group consisting of:
6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)-4-(5-phenylpyrazol-3-ylamino)-quinazoline and 264208-43-7 264207-90-1
6,7-dimethoxy-4-(5-phenylpyrazol-3-yloxy)quinazoline 264207-46-7
and pharmaceutically acceptable salts thereof.



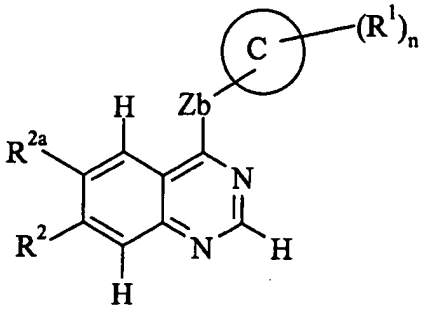
Claim 14 (**previously presented**): A compound as claimed in any one of claims 18 and 5 to 12 in the form of a pharmaceutically acceptable salt.

Claim 15 (**cancelled**).

Claim 16 (**previously presented**): A pharmaceutical composition which comprises as active ingredient a compound of formula II or a pharmaceutically acceptable salt thereof as claimed in any one of claims 18 and 5 to 12 in association with a pharmaceutically acceptable excipient or carrier.

Claim 17 (**previously presented**): A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a compound of formula II as defined in any one of claims 18 and 5 to 12 or a pharmaceutically acceptable salt thereof.

Claim 18 (**previously presented**): A compound of the formula II:



II

wherein:

ring C is a 5-6-membered heterocyclic moiety which may be saturated or unsaturated, which may be aromatic or non-aromatic, and which contains 1-3 heteroatoms selected independently from O, N and S;

Zb is –O- or –S-;

R^1 represents hydrogen, C_{1-4}alkyl, C_{1-4}alkoxymethyl, di(C_{1-4}alkoxy)methyl, C_{1-4}alkanoyl, trifluoromethyl, cyano, amino, C_{2-5}alkenyl, C_{2-5}alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C_{2-4}alkanoyl, C_{1-4}alkanoylamino, C_{1-4}alkoxycarbonyl, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphinyl, C_{1-4}alkylsulphonyl, carbamoyl, N-C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, aminosulphonyl, N-C_{1-4}alkylaminosulphonyl, N,N-di(C_{1-4}alkyl)aminosulphonyl, C_{1-4}alkylsulphonylamino, C_{1-4}alkylamino, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}haloalkyl, C_{1-4}hydroxyalkoxy, carboxy and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C_{1-4}alkoxycarbonyl; and additionally R^1 may represent carboxy, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-3}alkyl, or phenylC_{2-4}alkyl wherein the phenyl moiety may bear up to 5 substituents selected from the list herein defined for a phenyl ring which is directly linked to ring C;

n is an integer from 0 to 5;

m is an integer from 0 to 3;

R^2 represents hydroxy, cyano, nitro, trifluoromethyl, C_{1-3}alkylsulphanyl, -NR^3R^4 (wherein R^3 and R^4, which may be the same or different, each represents hydrogen or C_{1-3}alkyl), or R^5X^1- (wherein X^1 represents a direct bond, -O-, -CH_2-, -OCO-, carbonyl, -S-, -SO-,

$-SO_2-$, $-NR^6CO-$, $-CONR^7-$, $-SO_2NR^8-$, $-NR^9SO_2-$ or $-NR^{10}-$ (wherein R^6, R^7, R^8, R^9 and R^{10} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl), and R^5 is selected from one of the following eighteen groups:

1) hydrogen or C_{1-5}alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;

2) C_{1-5}alkylX^2COR^{11} (wherein X^2 represents -O- or $-NR^{12}-$ (in which R^{12} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{11} represents C_{1-3}alkyl, $-NR^{13}R^{14}$ or $-OR^{15}$ (wherein R^{13}, R^{14} and R^{15} which may be the same or different each represents hydrogen, C_{1-3}alkyl, C_{4-5}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

3) C_{1-5}alkylX^3R^{16} (wherein X^3 represents -O-, -S-, -SO-, $-SO_2-$, -OCO-, $-NR^{17}CO-$, $-CONR^{18}-$, $-SO_2NR^{19}-$, $-NR^{20}SO_2-$ or $-NR^{21}-$ (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen, C_{1-3}alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3}alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4}alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}cyanoalkyl and C_{1-4}alkoxycarbonyl);

4) C_{1-5}alkylX^4C_{1-5}alkylX^5R^{22} (wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, $-SO_2-$, $-NR^{23}CO-$, $-CONR^{24}-$, $-SO_2NR^{25}-$, $-NR^{26}SO_2-$ or $-NR^{27}-$ (wherein R^{23}, R^{24}, R^{25}, R^{26} and R^{27} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

5) R^{28} (wherein R^{28} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and C_{1-4}alkoxycarbonyl);

6) C_{1-5}alkylR^{28} (wherein R^{28} is as defined herein);

7) C_{2-5}alkenylR^{28} (wherein R^{28} is as defined herein);

8) C_{2-5}alkynylR^{28} (wherein R^{28} is as defined herein);

9) R^{29} (wherein R^{29} represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, trifluoromethyl, cyano, $-CONR^{30}R^{31}$ and $-NR^{32}COR^{33}$ (wherein R^{30}, R^{31}, R^{32} and R^{33}, which may be the same or different, each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

10) C_{1-5}alkylR^{29} (wherein R^{29} is as defined herein);

11) C_{2-5}alkenylR^{29} (wherein R^{29} is as defined herein);

12) C_{2-5}alkynylR^{29} (wherein R^{29} is as defined herein);

13) C_{1-5}alkylX^6R^{29} (wherein X^6 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{34}CO-$, $-CONR^{35}-$, $-SO_2NR^{36}-$, $-NR^{37}SO_2-$ or $-NR^{38}-$ (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

14) C_{2-5}alkenylX^7R^{29} (wherein X^7 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{39}CO-$, $-CONR^{40}-$, $-SO_2NR^{41}-$, $-NR^{42}SO_2-$ or $-NR^{43}-$ (wherein R^{39}, R^{40}, R^{41}, R^{42} and R^{43} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

15) C_{2-5}alkynylX^8R^{29} (wherein X^8 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{44}CO-$, $-CONR^{45}-$, $-SO_2NR^{46}-$, $-NR^{47}SO_2-$ or $-NR^{48}-$ (wherein R^{44}, R^{45}, R^{46}, R^{47} and R^{48} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

16) C_{1-3}alkylX^9C_{1-3}alkylR^{29} (wherein X^9 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{49}CO-$, $-CONR^{50}-$, $-SO_2NR^{51}-$, $-NR^{52}SO_2-$ or $-NR^{53}-$ (wherein R^{49}, R^{50}, R^{51}, R^{52} and R^{53} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

17) C_{1-3}alkylX^9C_{1-3}alkylR^{28} (wherein X^9 and R^{28} are as defined herein); and

18) C_{1-3}alkyl$R^{54}C_{1-3}$alkylX^9R^{55} (wherein X^9 is as defined herein and R^{54} and R^{55} are each independently selected from hydrogen, C_{1-3}alkyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3}alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4}alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}cyanoalkyl and C_{1-4}alkoxycarbonyl), with the proviso that R^{54} cannot be hydrogen;

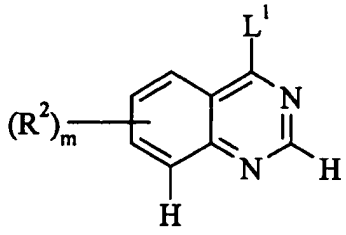
and additionally wherein any C_{1-5}alkyl, C_{2-5}alkenyl or C_{2-5}alkynyl group in R^5X^1- may bear one or more substituents selected from hydroxy, halogeno and amino; provided that R^2 is not hydrogen, substituted or unsubstituted C_{1-5}alkyl, C_{1-5}alkoxy, phenoxy or phenylC_{1-5}alkoxy; and

R^{2a} represents hydrogen, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, $-NR^{3a}R^{4a}$ (wherein R^{3a} and R^{4a}, which may be the same or different, each represents hydrogen or C_{1-3}alkyl), or $R^{5a}(CH_2)_{za}X^{1a}$ (wherein R^{5a} is a 5- or 6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl and C_{1-4}alkoxy, za is an integer from 0 to 4 and X^{1a} represents a direct bond, -O-, $-CH_2-$, -S-, -SO-, $-SO_2-$, $-NR^{6a}CO-$, $-CONR^{7a}-$, $-SO_2NR^{8a}-$, $-NR^{9a}SO_2-$ or $-NR^{10a}-$ (wherein R^{6a}, R^{7a}, R^{8a}, R^{9a} and R^{10a} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

or a salt thereof.

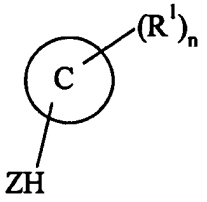
19 (**previously presented**): A process for the preparation of a compound of formula II or salt thereof, as defined in claim 18, which comprises:

(a) the reaction of a compound of the formula III:



(III)

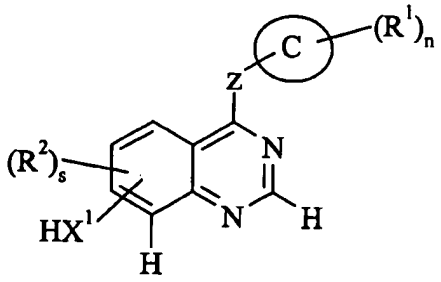
(wherein R^2 and m are as defined in claim 18 and L^1 is a displaceable moiety), with a compound of the formula IV:



(IV)

(wherein ring C, R^1, Z and n are as defined in claim 18);

(b) compounds of formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein R^5 is as defined in claim 18 and X^1 is -O-, -S-, -OCO- or -NR^{10}- (wherein R^{10} independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) may be prepared by the reaction of a compound of the formula V:



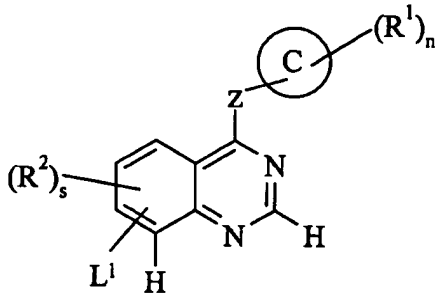
(V)

(wherein ring C, Z, R^1, R^2 and n are as defined in claim 18 and X^1 is as defined herein in this section and s is an integer from 0 to 2) with a compound of formula VI:

$$R^5\text{-}L^1 \qquad \text{(VI)}$$

(wherein R^5 is as defined in claim 18 and L^1 is as defined herein);

(c) compounds of the formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein R^5 is as defined in claim 18 and X^1 is -O-, -S-, -OCO- or -NR^{10}- (wherein R^{10} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) may be prepared by the reaction of a compound of the formula VII:



(VII)

with a compound of the formula VIII:

$$R^5\text{-}X^1\text{-}H \qquad \text{(VIII)}$$

(wherein R^1, R^2, R^5, ring C, Z and n are as defined in claim 18 and s and L^1 are as defined herein and X^1 is as defined herein in this section);

(d) compounds of the formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein X^1 is as defined in claim 18 and R^5 is C_{1-5}alkylR^{62}, wherein R^{62} is selected from one of the following nine groups:

1) $X^{10}C_{1-3}$alkyl (wherein X^{10} represents -O-, -S-, $-SO_2-$, $-NR^{63}CO-$ or $-NR^{64}SO_2-$ (wherein R^{63} and R^{64} which may be the same or different are each hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

2) $NR^{65}R^{66}$ (wherein R^{65} and R^{66} which may be the same or different are each hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

3) $X^{11}C_{1-5}$alkylX^5R^{22} (wherein X^{11} represents -O-, -S-, $-SO_2-$, $-NR^{67}CO-$, $-NR^{68}SO_2-$ or $-NR^{69}-$ (wherein R^{67}, R^{68}, and R^{69} which may be the same or different are each hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and X^5 and R^{22} are as defined in claim 18);

4) R^{28} (wherein R^{28} is as defined in claim 18);

5) $X^{12}R^{29}$ (wherein X^{12} represents -O-, -S-, $-SO_2-$, $-NR^{70}CO-$, $-NR^{71}SO_2-$, or $-NR^{72}-$ (wherein R^{70}, R^{71}, and R^{72} which may be the same or different are each hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined in claim 18);

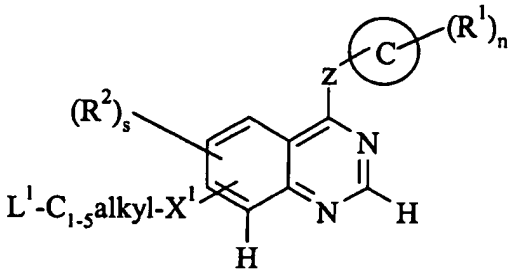
6) $X^{13}C_{1-5}$alkylR^{29}, preferably $X^{13}C_{1-3}$alkylR^{29}, (wherein X^{13} represents -O-, -S-, $-SO_2-$, $-NR^{73}CO-$, $-NR^{74}SO_2-$ or $-NR^{75}-$ (wherein R^{73}, R^{74} and R^{75} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined in claim 18);

7) R^{29} (wherein R^{29} is as defined in claim 18);

8) $X^{14}C_{1-3}$alkylR^{28} (wherein X^{14} represents -O-, -S-, $-SO_2-$, $-NR^{76}CO-$, $-NR^{77}SO_2-$ or $-NR^{78}-$ (wherein R^{76}, R^{77} and R^{78} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{28} is as defined in claim 18); and

9) $R^{54}C_{1-3}$alkylX^9R^{55} (wherein R^{54}, R^{55} and X^9 are as defined in claim 18);

may be prepared by reacting a compound of the formula IX:



(IX)

(wherein X^1, R^1, R^2, ring C, Z and n are as defined in claim 18 and s and L^1 are as defined herein) with a compound of the formula X:

$$R^{62}\text{-}H \qquad (X)$$

(wherein R^{62} is as defined herein);

(e) compounds of the formula II and salts thereof wherein one or more of the substituents $(R^2)_m$ is represented by $-NR^{79}R^{80}$, where one (and the other is hydrogen) or both of R^{79} and R^{80} are C_{1-3}alkyl, may be prepared by the reaction of compounds of formula II wherein the substituent $(R^2)_m$ is an amino group and an alkylating agent;

(f) compounds of the formula II and salts thereof wherein X^1 is -SO- or $-SO_2-$ may be prepared by oxidation from the corresponding compound in which X^1 is -S- or -SO-;

and when a salt of a compound of formula II is required, reaction of the compound obtained with an acid or base whereby to obtain the desired salt.

```
=> d que
L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-12-0
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-18-6
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-31-3
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-33-5
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-50-3
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-35-7
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-72-9
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-76-3
L9             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-54-7
L10            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-14-2
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-16-4
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-38-0
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-96-7
L14            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-98-9
L15            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-00-6
L16            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-74-1
L17            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-41-5
L18            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-68-3
L19            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264208-43-7
L20            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-90-1
L21            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  264207-46-7
L22           21 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5
                  OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR
                  L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21)
L23            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  (264207-46-7/CRN OR 264207-50
                  -3/CRN OR 264207-54-7/CRN OR 264207-68-3/CRN OR 264207-72-9/CRN
                   OR 264207-74-1/CRN OR 264207-76-3/CRN OR 264207-90-1/CRN OR
                  264207-96-7/CRN OR 264207-98-9/CRN OR 264208-00-6/CRN OR
                  264208-12-0/CRN OR 264208-14-2/CRN OR 264208-16-4/CRN OR
                  264208-18-6/CRN OR 264208-31-3/CRN OR 264208-33-5/CRN OR
                  264208-35-7/CRN OR 264208-38-0/CRN OR 264208-41-5/CRN OR
                  264208-43-7/CRN)
L24           28 SEA FILE=REGISTRY ABB=ON  PLU=ON  L23 OR L22
L25            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24


=> d l25 iall hitstr

L25  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2000:260277  HCAPLUS
DOCUMENT NUMBER:          132:293771
ENTRY DATE:               Entered STN:  21 Apr 2000
TITLE:                    Preparation of quinazolines as VEGF receptor tyrosine
                          kinase inhibitors
INVENTOR(S):              Hennequin, Laurent Francois Andre; Pasquet, Georges
PATENT ASSIGNEE(S):       Zeneca Limited, UK; Zeneca-Pharma S.A.
SOURCE:                   PCT Int. Appl., 107 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
INT. PATENT CLASSIF.:
            MAIN:         C07D403-12
       SECONDARY:         C07D401-14; C07D405-14; C07D403-14; A61K031-517
CLASSIFICATION:           28-16 (Heterocyclic Compounds (More Than One Hetero
                          Atom))
```

Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

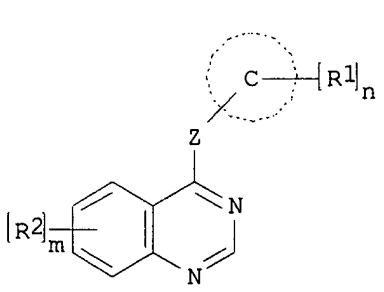
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021955	A1	20000420	WO 1999-GB3295	19991005
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344290	AA	20000420	CA 1999-2344290	19991005
AU 9961128	A1	20000501	AU 1999-61128	19991005
AU 756556	B2	20030116		
BR 9914326	A	20010626	BR 1999-14326	19991005
EP 1119567	A1	20010801	EP 1999-947758	19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527436	T2	20020827	JP 2000-575861	19991005
NZ 510434	A	20031031	NZ 1999-510434	19991005
ZA 2001002655	A	20020930	ZA 2001-2655	20010330
NO 2001001739	A	20010607	NO 2001-1739	20010406

PRIORITY APPLN. INFO.: EP 1998-402496 A 19981008
WO 1999-GB3295 W 19991005

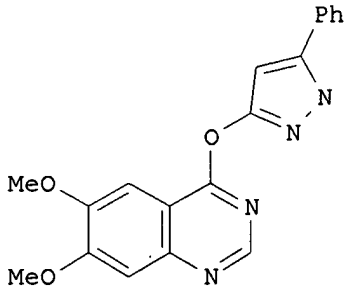
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000021955	ICM	C07D403-12
	ICS	C07D401-14; C07D405-14; C07D403-14; A61K031-517
WO 2000021955	ECLA	C07D401/14+239+231+213; C07D401/14+239+231+211; C07D403/12+239+231; C07D403/14+249+239+231; C07D521/00B1E2A

OTHER SOURCE(S): MARPAT 132:293771
GRAPHIC IMAGE:



I



II

ABSTRACT:

The title compds. [I; ring C = 5-6 membered heterocyclic moiety; Z = O, NH, S, CH2; R1 = H, alkyl, alkoxymethyl, etc.; n = 0-5; m = 0-3; R2 = H, OH, halo, etc.] and their salts which inhibit the effects of VEGF , and therefore useful in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals, were prepared and formulated. E.g., a multi-step synthesis of quinazoline II was given. Compds. I are effective at 1-50 mg/kg/day.

SUPPL. TERM: quinazoline prepn VEGF receptor tyrosine kinase inhibitor; angiogenesis inhibitor quinazoline prepn; vascular permeability quinazoline prepn

INDEX TERM: Blood vessel
(permeability, reducing; preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

INDEX TERM: Angiogenesis inhibitors
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

INDEX TERM: Vascular endothelial growth factor receptors
ROLE: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

INDEX TERM: **264207-46-7P** 264207-48-9P **264207-50-3P**
264207-52-5P **264207-54-7P**
264207-56-9P **264207-58-1P**
264207-60-5P **264207-62-7P**
264207-64-9P 264207-66-1P **264207-68-3P**
264207-70-7P **264207-72-9P** **264207-74-1P**
264207-76-3P 264207-78-5P 264207-80-9P
264207-82-1P 264207-84-3P 264207-86-5P 264207-88-7P
264207-90-1P 264207-92-3P **264207-94-5P**
264207-96-7P **264207-98-9P**
264208-00-6P 264208-02-8P 264208-04-0P
264208-06-2P 264208-08-4P 264208-10-8P
264208-12-0P **264208-14-2P**
264208-16-4P **264208-18-6P** 264208-21-1P
264208-23-3P 264208-26-6P 264208-28-8P
264208-31-3P **264208-33-5P**
264208-35-7P **264208-38-0P**
264208-41-5P **264208-43-7P**
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

INDEX TERM: 104-97-2, 3-Cyclopentylpropionyl chloride 109-01-3, 1-Methylpiperazine 109-70-6, 1-Bromo-3-chloropropane 109-86-4, 2-Methoxyethanol 111-77-3, 2-(2-Methoxyethoxy)ethanol 121-34-6, 4-Hydroxy-3-methoxybenzoic acid 446-32-2, 2-Amino-4-fluorobenzoic acid 617-05-0, Ethyl 4-hydroxy-3-methoxybenzoate 838-57-3, Ethyl 4-nitrobenzoylacetate 1126-09-6, Ethyl 4-piperidinecarboxylate 1479-24-9, Ethyl 2-fluorobenzoylacetate 1572-10-7 1615-14-1, 1H-Imidazole-1-ethanol 2033-24-1, 2,2-Dimethyl-1,3-dioxane-4,6-dione 2058-49-3 2881-63-2, Ethyl

4-chlorobenzoylacetate 2881-83-6, Ethyl
4-methoxybenzoylacetate 3249-68-1 4687-37-0, Ethyl
3,4-dimethoxybenzoylacetate 4860-93-9 5653-40-7,
4,5-Dimethoxyanthranilic acid 6283-81-4 6482-24-2,
2-Bromoethyl methyl ether 7357-67-7, 3-Morpholinopropyl
chloride 18997-19-8, Chloromethyl pivalate 19541-95-8
24979-46-2 26377-17-3, Ethyl isonicotinoylacetate
35087-28-6 35087-29-7 36878-91-8, Ethyl 3-furoylacetate
52119-38-7, Ethyl 3-nitrobenzoylacetate 55120-06-4
60547-98-0, 2-Amino-4-benzyloxy-5-methoxybenzamide
63131-29-3, Methyl 4-fluorobenzoylacetate 74731-63-8,
2-(1,2,3-Triazol-1-yl)ethanol 78583-81-0 78597-54-3
208519-10-2 209224-91-9 264209-14-5 264209-16-7
264209-19-0 264209-20-3 264209-22-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

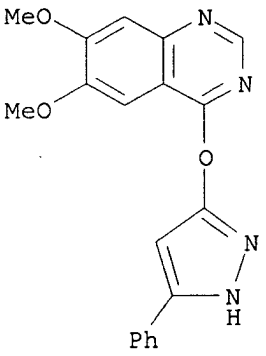
INDEX TERM: 1578-89-8P 4891-32-1P 13790-39-1P, 4-Chloro-6,7-dimethoxyquinazoline 13794-72-4P 16499-57-3P
29211-70-9P 50931-94-7P 54945-13-0P 59719-19-6P
69678-02-0P 101421-76-5P 123855-51-6P 142851-03-4P
166815-96-9P 179688-01-8P 193002-24-3P 193002-25-4P
193002-30-1P 193002-31-2P 193002-32-3P 196194-41-9P
196194-42-0P 196194-43-1P 196194-44-2P 196194-45-3P
196194-62-4P 196194-86-2P 196194-88-4P 196195-13-8P
196603-84-6P 196603-85-7P 196603-86-8P 196603-87-9P
199327-54-3P 199328-74-0P 199328-77-3P 199328-78-4P
220896-22-0P 220896-27-5P 220896-29-7P 264208-45-9P
264208-47-1P 264208-49-3P 264208-51-7P 264208-53-9P
264208-55-1P 264208-58-4P 264208-60-8P 264208-63-1P
264208-66-4P 264208-69-7P 264208-72-2P 264208-79-9P
264208-83-5P 264208-86-8P 264208-89-1P 264208-92-6P
264208-95-9P 264208-98-2P 264209-01-0P 264209-04-3P
264209-07-6P 264209-09-8P 264209-11-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD.

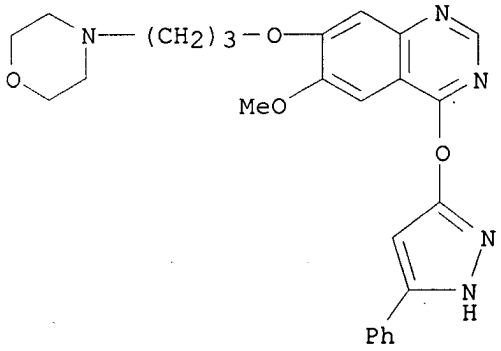
REFERENCE(S): (1) Glaxo; WO 9935132 A 1999 HCAPLUS
(2) Rhone-Poulenc; WO 9515758 A 1995 HCAPLUS
(3) Rhone-Poulenc; WO 9639145 A 1996 HCAPLUS

IT **264207-46-7P 264207-50-3P 264207-52-5P**
264207-54-7P 264207-56-9P 264207-58-1P
264207-60-5P 264207-62-7P 264207-64-9P
264207-68-3P 264207-72-9P 264207-74-1P
264207-76-3P 264207-90-1P 264207-94-5P
264207-96-7P 264207-98-9P 264208-00-6P
264208-12-0P 264208-14-2P 264208-16-4P
264208-18-6P 264208-31-3P 264208-33-5P
264208-35-7P 264208-38-0P 264208-41-5P
264208-43-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

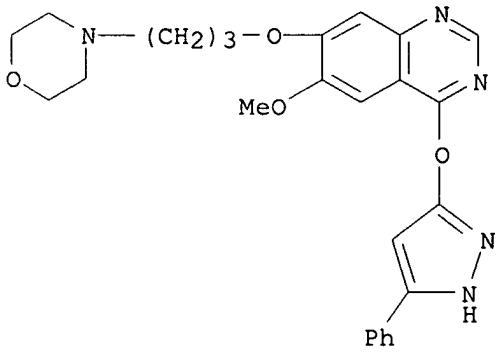
RN 264207-46-7 HCAPLUS
CN Quinazoline, 6,7-dimethoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



RN 264207-50-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

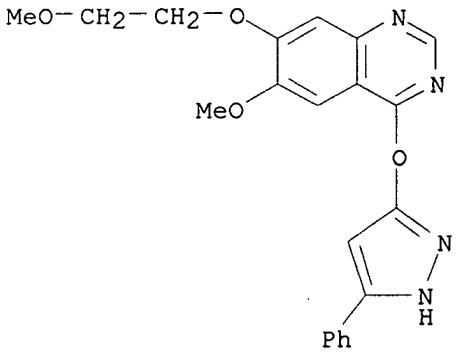


RN 264207-52-5 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, dihydrochloride (9CI) (CA INDEX NAME)

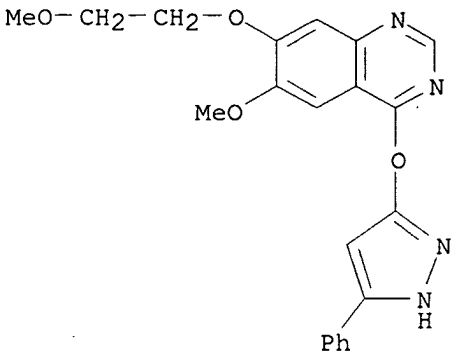


●2 HCl

RN 264207-54-7 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

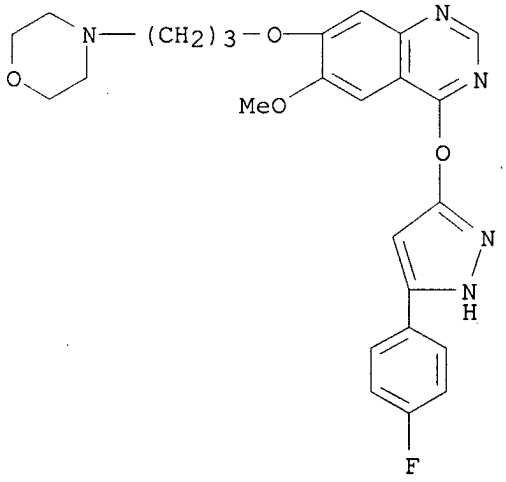


RN 264207-56-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (4:3) (9CI) (CA INDEX NAME)



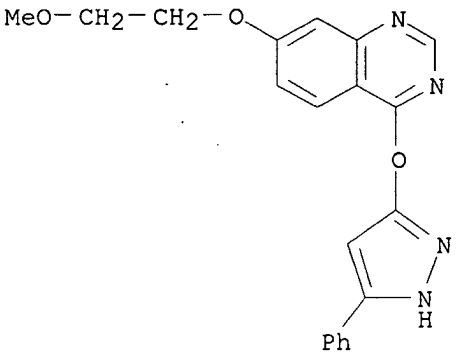
●3/4 HCl

RN 264207-58-1 HCAPLUS
CN Quinazoline, 4-[[5-(4-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)



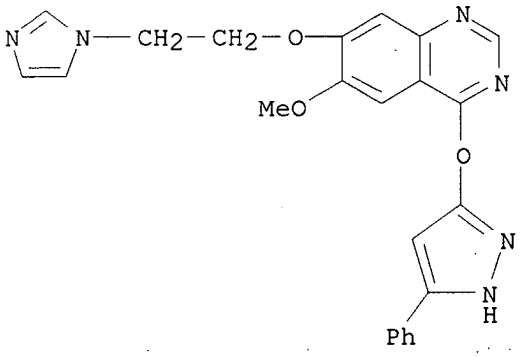
●19/10 HCl

RN 264207-60-5 HCAPLUS
CN Quinazoline, 7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (5:3) (9CI) (CA INDEX NAME)



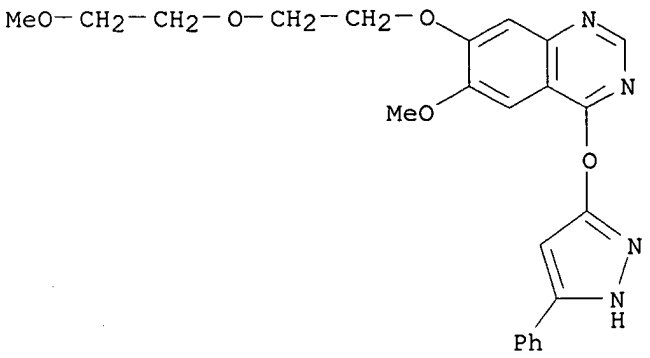
●3/5 HCl

RN 264207-62-7 HCAPLUS
CN Quinazoline, 7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (2:5) (9CI) (CA INDEX NAME)



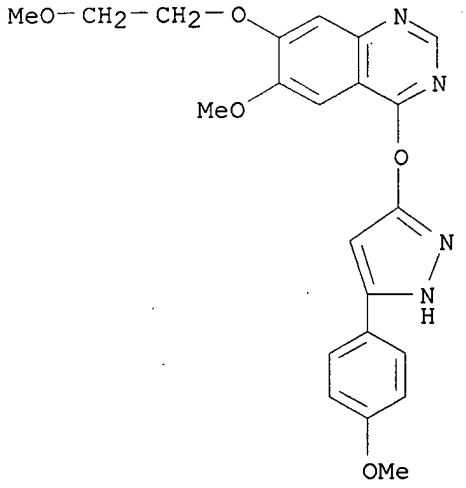
●5/2 HCl

RN 264207-64-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (20:17) (9CI) (CA INDEX NAME)

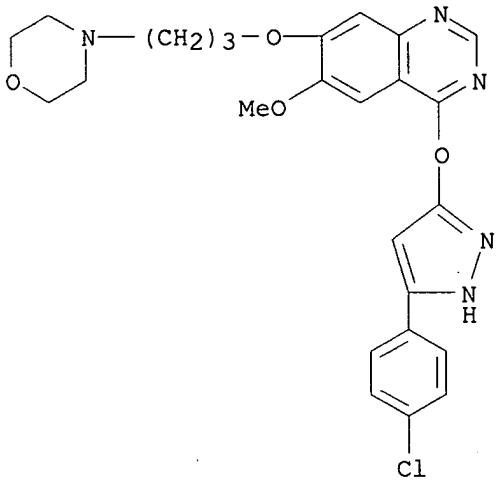


●17/20 HCl

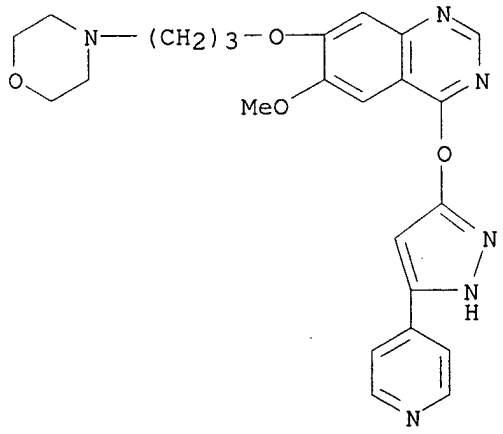
RN 264207-68-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



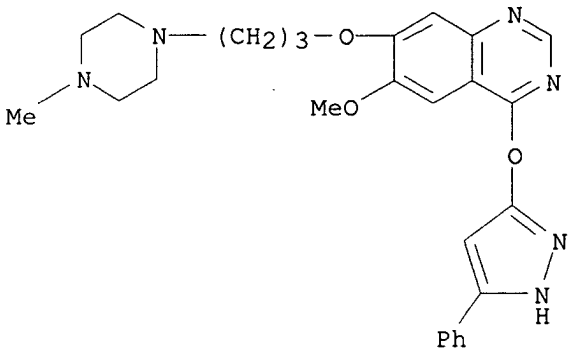
RN 264207-72-9 HCAPLUS
CN Quinazoline, 4-[[5-(4-chlorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



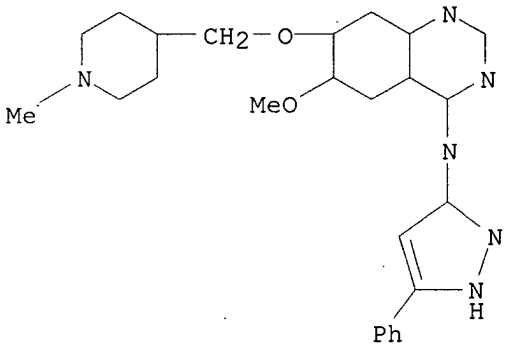
RN 264207-74-1 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(4-pyridinyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



RN 264207-76-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

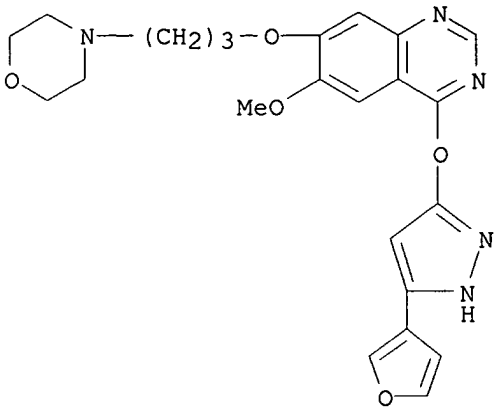


RN 264207-90-1 HCAPLUS
CN 4-Quinazolinamine, 6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]-N-(5-phenyl-1H-pyrazol-3-yl)-, hydrochloride (5:12) (9CI) (CA INDEX NAME)



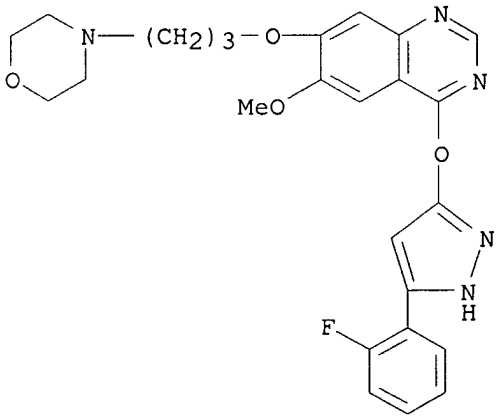
●12/5 HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 264207-94-5 HCAPLUS
CN Quinazoline, 4-[[5-(3-furanyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]-, hydrochloride (9CI) (CA INDEX NAME)

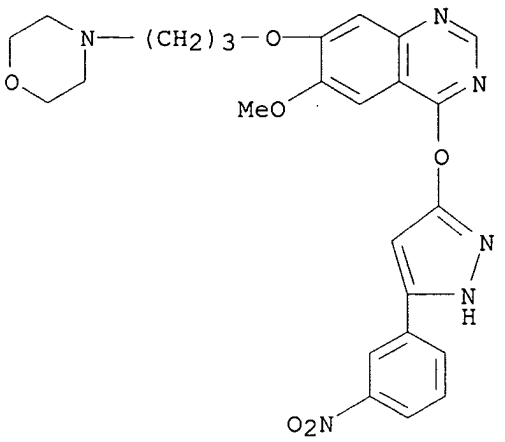


● x HCl

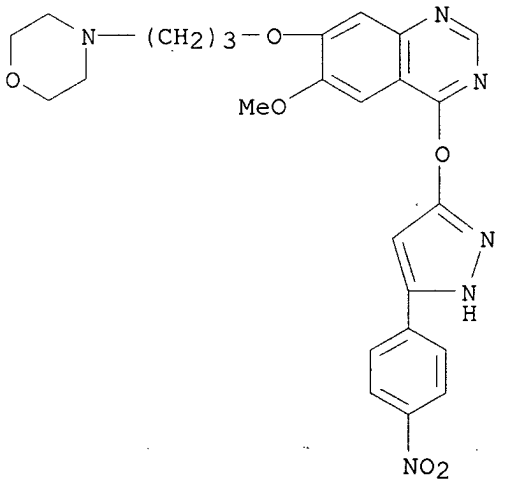
RN 264207-96-7 HCAPLUS
CN Quinazoline, 4-[[5-(2-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



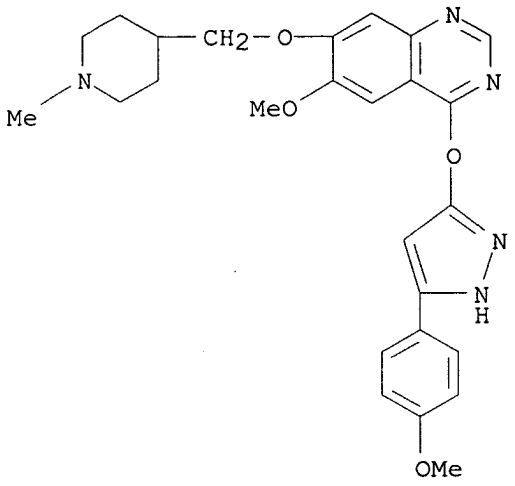
RN 264207-98-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(3-nitrophenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



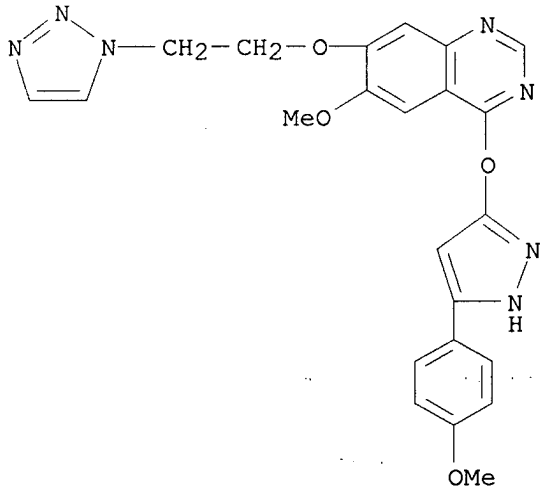
RN 264208-00-6 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(4-nitrophenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



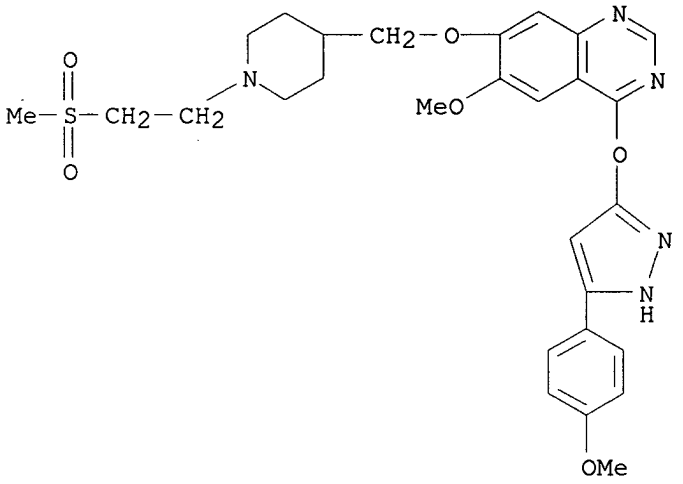
RN 264208-12-0 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[(1-methyl-4-piperidinyl)methoxy]- (9CI) (CA INDEX NAME)



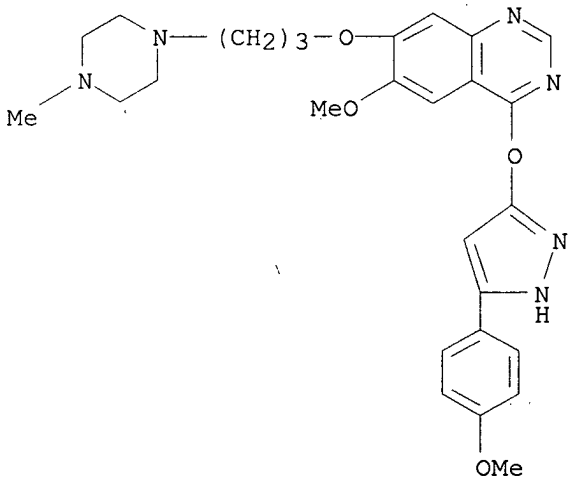
RN 264208-14-2 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]- (9CI) (CA INDEX NAME)



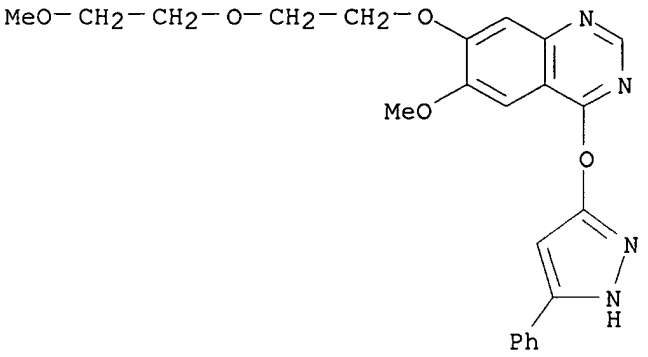
RN 264208-16-4 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[[1-[2-(methylsulfonyl)ethyl]-4-piperidinyl]methoxy]- (9CI) (CA INDEX NAME)



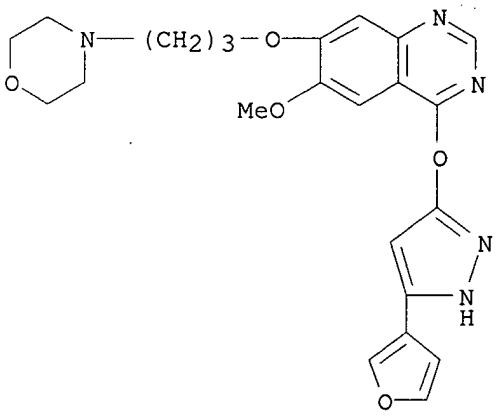
RN 264208-18-6 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



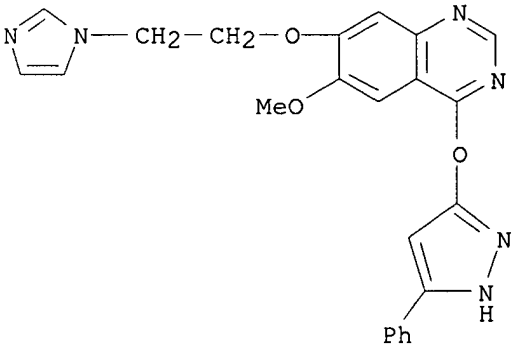
RN 264208-31-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



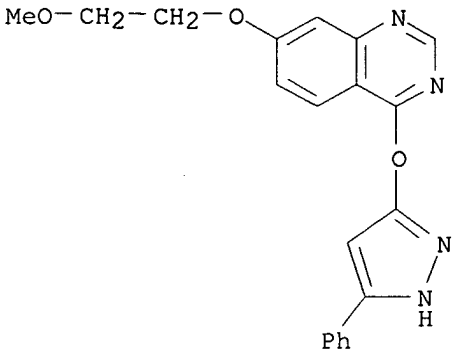
RN 264208-33-5 HCAPLUS
CN Quinazoline, 4-[[5-(3-furanyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



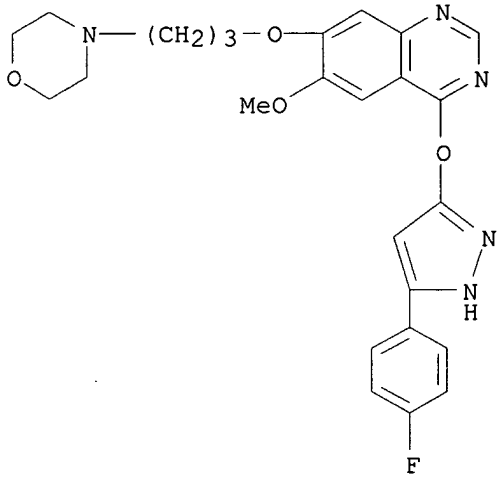
RN 264208-35-7 HCAPLUS
CN Quinazoline, 7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



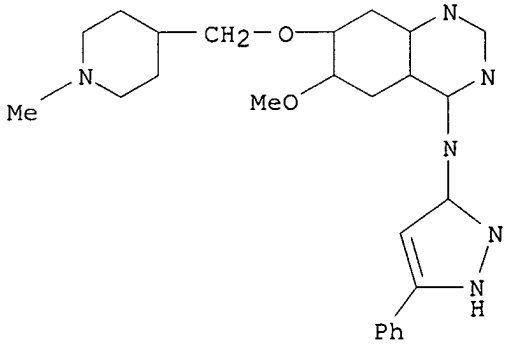
RN 264208-38-0 HCAPLUS
CN Quinazoline, 7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



RN 264208-41-5 HCAPLUS
CN Quinazoline, 4-[[5-(4-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)

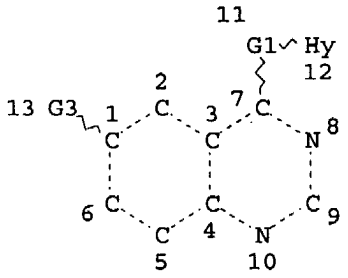


RN 264208-43-7 HCAPLUS
CN 4-Quinazolinamine, 6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]-N-(5-phenyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

```
=> d que
L27                 STR
```



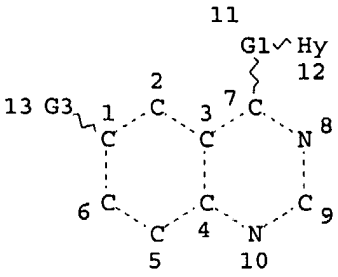
Ak @14 S Ak @15 16 NH Ak @17 18 O Ak @19 20

Ak N Ak
21 @22 23

```
VAR G1=O/S
VAR G3=H/X/14/19/15/NH2/17/22
NODE ATTRIBUTES:
CONNECT IS E2  RC AT   2
CONNECT IS E2  RC AT   5
CONNECT IS E2  RC AT   9
CONNECT IS E1  RC AT  14
CONNECT IS E2  RC AT  15
CONNECT IS E2  RC AT  16
CONNECT IS E1  RC AT  18
CONNECT IS E1  RC AT  20
CONNECT IS E1  RC AT  21
CONNECT IS E1  RC AT  23
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  AT  12
GGCAT   IS LOC  AT  14
GGCAT   IS LOC  AT  16
GGCAT   IS LOC  AT  18
GGCAT   IS LOC  AT  20
GGCAT   IS LOC  AT  21
GGCAT   IS LOC  AT  23
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
L29          119 SEA FILE=REGISTRY SSS FUL L27
L33              STR
```



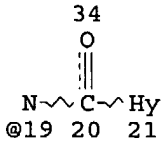
S Hy
@17 18

O C N Hy
22 @23 24 25

S N Hy
@26 27 28

N S Hy
@29 30 31

N Hy
@32 33



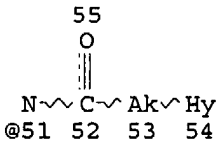
Ak Hy
@35 36

O Ak Hy
@37 38 39

S Ak Hy
@40 41 42

N Ak Hy
@43 44 45

O C N Ak Hy
46 @47 48 49 50



N S Ak Hy
@56 57 58 59

S N Ak Hy
@60 61 62 63

Hy @64

O Hy
@65 66

VAR G1=O/S
VAR G3=17/23/26/29/32/19/35/37/40/43/47/51/56/60/64/65
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 2
CONNECT IS E2 RC AT 5
CONNECT IS E2 RC AT 9
CONNECT IS E2 RC AT 35
CONNECT IS E2 RC AT 38
CONNECT IS E2 RC AT 41
CONNECT IS E2 RC AT 44
CONNECT IS E2 RC AT 49
CONNECT IS E2 RC AT 53
CONNECT IS E2 RC AT 58
CONNECT IS E2 RC AT 62
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY AT 12
GGCAT IS MCY SAT AT 18
GGCAT IS MCY SAT AT 21
GGCAT IS MCY SAT AT 25
GGCAT IS MCY SAT AT 28
GGCAT IS MCY SAT AT 31
GGCAT IS MCY SAT AT 33
GGCAT IS LIN SAT AT 35
GGCAT IS MCY SAT AT 36
GGCAT IS LIN SAT AT 38
GGCAT IS MCY SAT AT 39
GGCAT IS LIN SAT AT 41
GGCAT IS MCY SAT AT 42
GGCAT IS LIN SAT AT 44
GGCAT IS MCY SAT AT 45

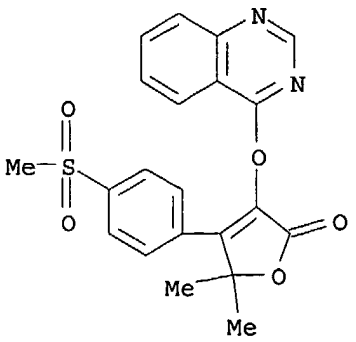
```
GGCAT   IS LIN  SAT  AT  49
GGCAT   IS MCY  SAT  AT  50
GGCAT   IS LIN  SAT  AT  53
GGCAT   IS MCY  SAT  AT  54
GGCAT   IS LIN  SAT  AT  58
GGCAT   IS MCY  SAT  AT  59
GGCAT   IS LIN  SAT  AT  62
GGCAT   IS MCY  SAT  AT  63
GGCAT   IS MCY  SAT  AT  64
GGCAT   IS MCY  SAT  AT  66
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  63

STEREO ATTRIBUTES: NONE
L35           0 SEA FILE=REGISTRY SSS FUL L33
L36         119 SEA FILE=REGISTRY ABB=ON  PLU=ON  L29 OR L35
L38          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36
L39          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36(L)PREP/RL
L40          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L39


=> d l40 ibib abs hitstr 1-24

L40  ANSWER 1 OF 24  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:815644  HCAPLUS
DOCUMENT NUMBER:          141:420034
TITLE:                    Quantitative structure activity relationship studies
                          of diaryl furanones as selective COX-2 inhibitors
AUTHOR(S):                Shahapurkar, S.; Pandya, T.; Kawathekar, N.;
                          Chaturvedi, S. C.
CORPORATE SOURCE:         Devi Ahilya Vishwavidyalaya, Takshashila Parisar,
                          School of Pharmacy, Indore, India
SOURCE:                   European Journal of Medicinal Chemistry (2004),
                          39(10), 899-904
                          CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Selective COX-2 inhibitors have attracted much attention in recent times
     in the design of non-steroidal anti-inflammatory agents (NSAID), which are
     devoid of the common side effects of classical NSAIDs.  QSAR studies have
     been performed on a series of diaryl furanones that acts as selective
     COX-2 inhibitor using Mol. Operating Environment (MOE).  The studies were
     carried out on 43 analogs.  These studies produced good predictive models
     and give statistically significant correlations of selective COX-2
     inhibitory with phys. property, connectivity and conformation of mol.
     Also when available COX-1 inhibitory data was analyzed with descriptors
     obtained from MOE, partial charge descriptor, van der Waal's surface area
     and solvation energy gave statistically significant results.
IT   189955-00-8
     RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
     use); BIOL (Biological study); USES (Uses)
        (QSAR studies of diaryl furanones as selective COX-2 inhibitors)
RN   189955-00-8  HCAPLUS
CN   2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-
     quinazolinyloxy)- (9CI)  (CA INDEX NAME)
```

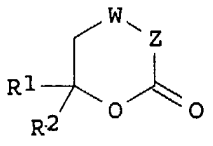


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

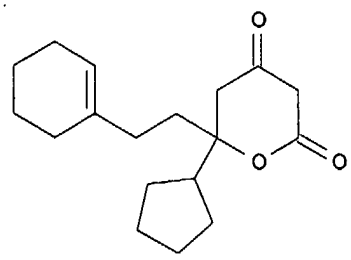
L40 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:718528 HCAPLUS
DOCUMENT NUMBER: 141:243338
TITLE: Preparation of tetrahydropyranones as hepatitis C virus RNA-dependent RNA polymerase inhibitors
INVENTOR(S): Borchardt, Allen John; Gonzalez, Javier; Li, Hui; Linton, Maria Angelica; Tatlock, John Howard
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 527 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004074270	A2	20040902	WO 2004-IB493		20040209
WO 2004074270	A3	20041223			
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004224960	A1	20041111	US 2004-783117		20040217
NL 1025544	A1	20040824	NL 2004-1025544		20040220
PRIORITY APPLN. INFO.:			US 2003-449088P	P	20030221
			US 2003-472355P	P	20030520

OTHER SOURCE(S): MARPAT 141:243338
GI



I



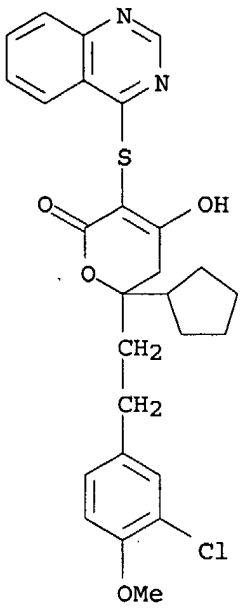
II

AB Title compds. I [wherein WZ = COCHR3, C(OR6)=CR3'; R1 = independently H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, or aryl; R2 = R1, (un)substituted arylalkyl, heterocyclylalkyl, arylalkoxy, or heterocyclylalkoxy, etc.; R3 = H, OR6, SR6, NR6R7, R2; R3' = R3 except H; R6, R7 = independently H, (un)substituted (cyclo)alkyl, aryl(alkyl), or heterocyclyl(alkyl); and pharmaceutically acceptable salts, solvates, prodrugs, and metabolites thereof], including purine derivs., were prepared as hepatitis C virus (HCV) RNA-dependent RNA polymerase (RdRp) inhibitors. For example, 3-(cyclohex-1-enyl)propionic acid Et ester was hydrolyzed with LiOH in THF/MeOH to give the acid, which was esterified with 2,2'-dipyridyl disulfide in CH2CH2 to provide 3-(cyclohex-1-enyl)thiopropionic acid S-(pyridin-2-yl) ester (93%). Reaction of the thioester with cyclopentylmagnesium bromide in THF afforded 3-(cyclohex-1-enyl)-1-cyclopentylpropan-1-one (72%). Coupling of the ketone with Me acetoacetate in the presence of NaH and BuLi in THF produced the 2,4-pyrandione II (40%). Compds. of the invention inhibited the ability of recombinant HCV polymerase to perform primer/template-directed transcription in vitro with IC50 values ranging from 0.001 μM to 83 μM. Thus, I and pharmaceutical compns. are useful for treating Hepatitis C virus in mammals (no data).

IT **749933-73-1P**, 6-[2-(3-Chloro-4-methoxyphenyl)ethyl]-6-cyclopentyl-4-hydroxy-3-[(quinazolin-4-yl)thio]-5,6-dihydro-2H-pyran-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(HCV polymerase inhibitor; preparation of pyranones as HCV polymerase inhibitors)

RN 749933-73-1 HCAPLUS

CN 2H-Pyran-2-one, 6-[2-(3-chloro-4-methoxyphenyl)ethyl]-6-cyclopentyl-5,6-dihydro-4-hydroxy-3-(4-quinazolinylthio)- (9CI) (CA INDEX NAME)

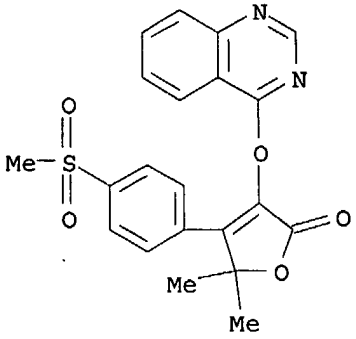


L40 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:303493 HCAPLUS
DOCUMENT NUMBER: 141:16893
TITLE: Quantitative structure activity relationship studies of diaryl furanones as selective COX-2 inhibitors
AUTHOR(S): Shahapurkar, S.; Pandya, T.; Kawathekar, N.; Chaturvedi, S. C.
CORPORATE SOURCE: School of Pharmacy, Indore, India
SOURCE: European Journal of Medicinal Chemistry (2004), 39(4), 383-388
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Selective COX-2 inhibitors have attracted much attention in recent times in the design of non-steroidal anti-inflammatory agents (NSAID), which are devoid of the common side effects of classical NSAIDs. QSAR studies have been performed on a series of diaryl furanones that acts as selective COX-2 inhibitor using Mol. Operating Environment (MOE). The studies were carried out on 43 analogs. These studies produced good predictive models and give statistically significant correlations of selective COX-2 inhibitory with phys. property, connectivity and conformation of mol. Also when available COX-1 inhibitory data was analyzed with descriptors obtained from MOE, partial charge descriptor, van der Waal's surface area and solvation energy gave statistically significant results.

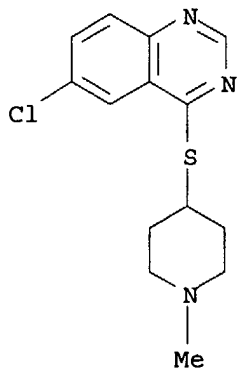
IT **189955-00-8**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quant. structure activity relationship studies of diaryl furanones as selective COX-2 inhibitors)

RN 189955-00-8 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:205966 HCAPLUS
TITLE: Product class 13: quinazolines
AUTHOR(S): Kikelj, D.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2004), 16, 573-749
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Preparation of quinazolines by ring closure and ring transformation reactions as well as aromatization and substituent modification is given.
IT INDEXING IN PROGRESS
IT **325145-98-0P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of quinazolines)
RN 325145-98-0 HCAPLUS
CN Quinazoline, 6-chloro-4-[(1-methyl-4-piperidinyl)thio]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1014 THERE ARE 1014 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

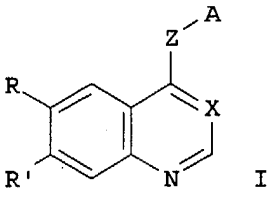
L40 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182845 HCAPLUS

DOCUMENT NUMBER: 140:217519
TITLE: Preparation of quinoline derivatives as TGFβ inhibitors
INVENTOR(S): Shimizu, Kiyoshi; Shimizu, Toshiyuki; Kimura, Kaname; Kawakami, Kazuki; Nakoji, Masayoshi
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 628 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018430	A1	20040304	WO 2003-JP10647	20030822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-244028 A 20020823
OTHER SOURCE(S): MARPAT 140:217519
GI

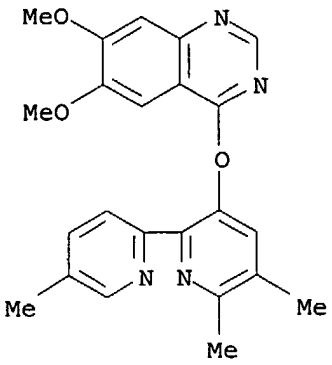


I

AB The title compds. I [wherein X = CH or N; Z = O, NH, S, or CO; R and R' = independently H, halo, (un)substituted alkyl, alkenyl, NH2, CONH2, OH, or heterocyclyl; A = (un)substituted Ph or (hetero)cyclyl] or pharmaceutically acceptable salts, or solvates thereof are prepared as transforming growth factor (TGF) β inhibitors. For example, 4-chloro-6,7-dimethoxyquinoline was reacted with 2-benzylphenol in 1,2-dichlorobenzene to give 4-(2-benzylphenoxy)-6,7-dimethoxyquinoline (10%). Some of compds. I inhibited 100% of human TGFβ at 10 μM.

IT **666734-04-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of quinoline derivs. as TGFβ inhibitors)

RN 666734-04-9 HCAPLUS
CN Quinazoline, 6,7-dimethoxy-4-[(5,5',6-trimethyl[2,2'-bipyridin]-3-yl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:162461 HCAPLUS
DOCUMENT NUMBER: 140:217653
TITLE: Preparation of heterocyclic-substituted quinolines/quinazolines and related compounds as Inhibitors of JAK protein kinase
INVENTOR(S): Bemis, Guy W.; Harbeson, Scott L.; Ledeboer, Mark
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 58 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004038992	A1	20040226	US 2003-430805	20030506
WO 2004058753	A1	20040715	WO 2003-US14223	20030506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1501829	A1	20050202	EP 2003-799762	20030506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-378185P P 20020506
WO 2003-US14223 A 20030506

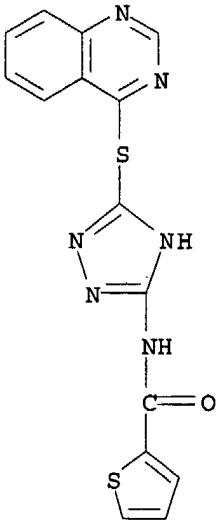
OTHER SOURCE(S): MARPAT 140:217653
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

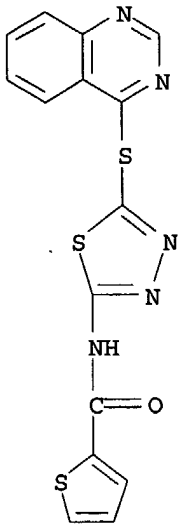
AB Title compds. I [W, X = O, S; A = N, CH, CCN, C-alkyl; R1-2 = taken together form an (un)substituted 3-7 membered (un)saturated (hetero)cycle; Q = bond, CO, carboxamido, etc.; R3 = alkyl, (un)substituted 3-8 membered monocyclic or 8-10 membered bicyclic ring, etc.] are prepared For instance, 5-((7-chloroquinolin-4-yl)oxy)-1,3,4-thiadiazole-2-carboxylic acid N-((furan-2-yl)methyl)amide (II) is prepared from ((furan-2-yl)methyl)amine and the corresponding thiadiazole Et ester (DME, 80°, 18 h). Certain example compds. have IC50 between 2 and 5 μM for JAK kinase. I are useful in the treatment of a neurodegenerative disorder, an autoimmune disorder, etc.

IT **664324-74-7P 664324-81-6P 664325-06-8P 664325-07-9P 664325-13-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of heterocyclic-substituted quinolines/quinazolines and related compds. as Inhibitors of jak protein kinase)

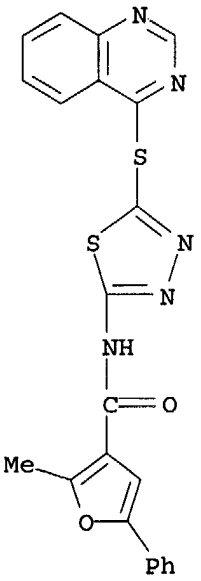
RN 664324-74-7 HCAPLUS
CN 2-Thiophenecarboxamide, N-[5-(4-quinazolinylthio)-1H-1,2,4-triazol-3-yl]- (9CI) (CA INDEX NAME)



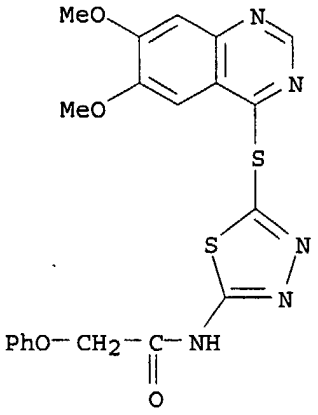
RN 664324-81-6 HCAPLUS
CN 2-Thiophenecarboxamide, N-[5-(4-quinazolinylthio)-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



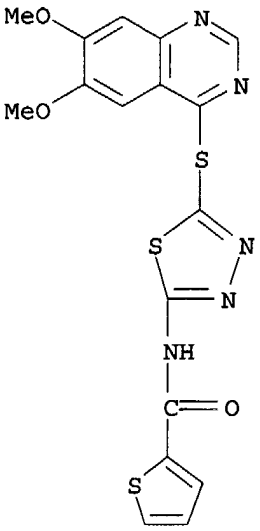
RN 664325-06-8 HCAPLUS
CN 3-Furancarboxamide, 2-methyl-5-phenyl-N-[5-(4-quinazolinylthio)-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



RN 664325-07-9 HCAPLUS
CN Acetamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)thio]-1,3,4-thiadiazol-2-yl]-2-phenoxy- (9CI) (CA INDEX NAME)



RN 664325-13-7 HCAPLUS
CN 2-Thiophenecarboxamide, N-[5-[(6,7-dimethoxy-4-quinazolinyl)thio]-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



L40 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:837079 HCAPLUS
DOCUMENT NUMBER: 139:338195
TITLE: Preparation of peptides as inhibitors of serine proteases, particularly HCV NS3-NS4A protease
INVENTOR(S): Pitlik, Janos; Cottrell, Kevin M.; Farmer, Luc J.; Perni, Robert B.; Courtney, Lawrence F.; Van Drie, John H.; Murcko, Mark A.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087092	A2	20031023	WO 2003-US11459	20030411
WO 2003087092	A3	20040910		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

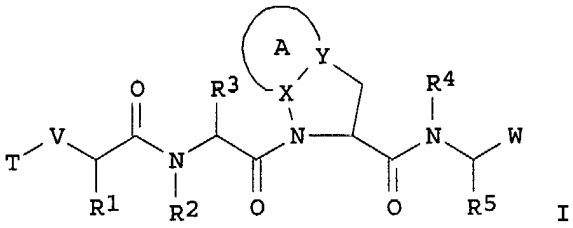
EP 1497282	A2	20050119	EP 2003-719741	20030411

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

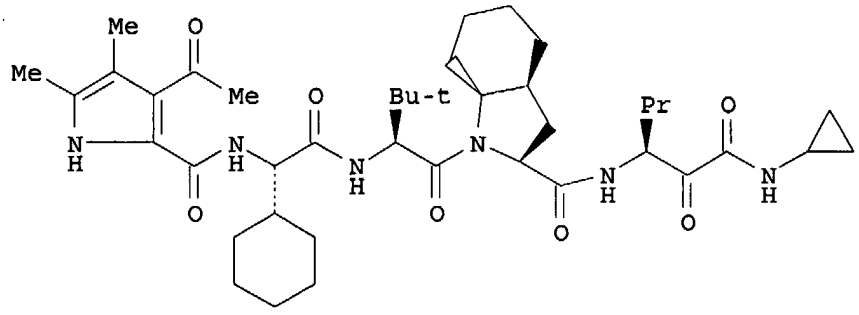
PRIORITY APPLN. INFO.:	US 2002-371846P	P	20020411
	WO 2003-US11459	W	20030411

OTHER SOURCE(S): MARPAT 139:338195

GI



I

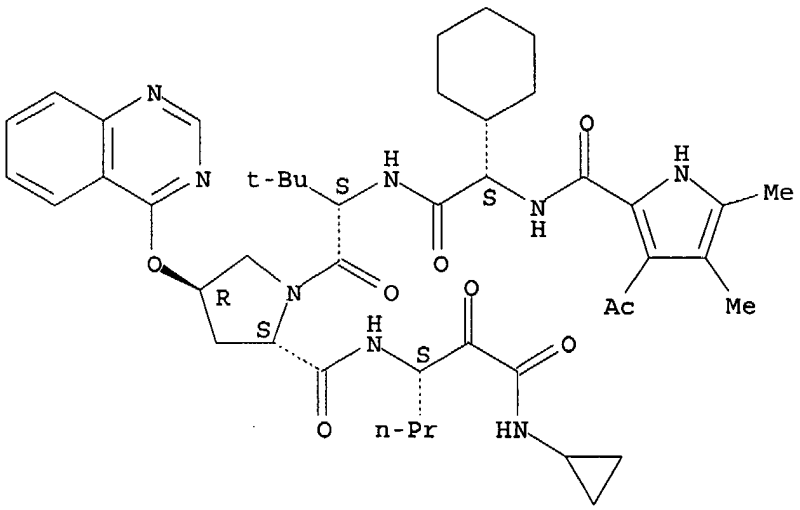


II

AB The invention relates to compds. I [A together with X and Y is a 3- to 6-membered aromatic or non-aromatic ring having up to 3 heteroatoms; R1, R3 are aliphatic, (un)substituted (cyclo)alk(en)yl, (hetero)aryl, etc.; R2, R4 are H, (un)substituted aliphatic, cycloalkyl or aryl aliphatic; R5 is (un)substituted aliphatic; W is COCOR6, COCO2R6, or COCONR62, where R6 is H, aliphatic, (hetero)aryl, etc.; V is CONR8, SONR8, SO2NR8, where R8 is H or aliphatic; T is (hetero)aryl, aliphatic, sulfonylaminoalkyl, etc.] that inhibit serine protease activity, particularly the activity of hepatitis C virus NS3-NS4A protease. Thus, peptide II was prepared via coupling reactions in solution and showed Ki and IC50 values < 0.5 μM.

IT **615584-04-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptides as inhibitors of serine proteases, particularly HCV NS3-NS4A protease)
RN 615584-04-8 HCAPLUS
CN L-Prolinamide, 3-acetyl-2,3,4,5-tetradehydro-4,5-dimethylprolyl-(2S)-2-cyclohexylglycyl-3-methyl-L-valyl-N-[(1S)-1-[(cyclopropylamino)oxoacetyl]butyl]-4-(4-quinazolinyloxy)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:276519 HCAPLUS
DOCUMENT NUMBER: 136:310188
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and an NSAID compound
INVENTOR(S): Heimbrook, David C.; Yao, Siu-long
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 129 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002042375	A1	20020411	US 2001-896245		20010629
PRIORITY APPLN. INFO.:			US 2000-216217P	P	20000705

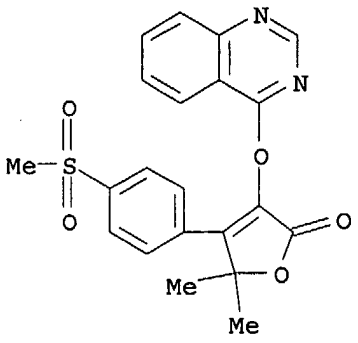
OTHER SOURCE(S): MARPAT 136:310188
AB The invention relates to methods of treating cancer using a combination of a compound which is a PSA conjugate and a nonsteroidal antiinflammatory agent (NSAID) and to methods of preparing such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg

= cyclohexylglycine) and COX-2 inhibitor 3-phenyl-4-[4-(4-methylsulfonyl)phenyl]-2(5H)furanone is an example of an NSAID compound (syntheses given).

IT **189955-00-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compound)

RN 189955-00-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



L40 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:860680 HCAPLUS

DOCUMENT NUMBER: 134:157196

TITLE: Synthesis and analgesic activity of some quinazoline analogs of anpirtoline

AUTHOR(S): Radl, Stanislav; Hezky, Petr; Proska, Jan; Krejci, Ivan

CORPORATE SOURCE: Research Institute of Pharmacy and Biochemistry, Prague, 13060, Czech Rep.

SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2000), 333(11), 381-386
CODEN: ARPMAS; ISSN: 0365-6233

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

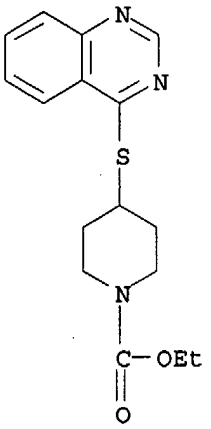
OTHER SOURCE(S): CASREACT 134:157196

AB New condensed derivs. of anpirtoline, in which the pyridine ring is replaced with quinoline, quinazoline, 7-chloroquinoline, and 7-chloroquinazoline nuclei, have been synthesized. Their receptor binding profiles (5-HT1A, 5-HT1B) and analgesic activity (hot plate, acetic acid induced writhing) have been studied. The analgesic activity of some of the compds. are comparable to that of clin. used drugs flupirtine and tramadol under the same conditions.

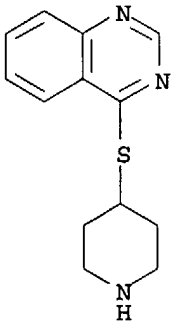
IT **232618-27-8P 232618-31-4P 232618-36-9P**
325145-97-9P 325145-98-0P 325145-99-1P
325146-00-7P 325146-01-8P 325146-02-9P
325146-03-0P 325146-04-1P 325146-05-2P
325146-06-3P 325146-07-4P 325146-08-5P
325146-09-6P 325146-10-9P 325146-11-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(synthesis and analgesic activity of quinazoline analogs of anpirtoline)

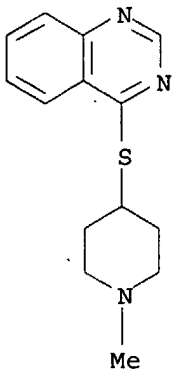
RN 232618-27-8 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, ethyl ester (9CI) (CA INDEX NAME)



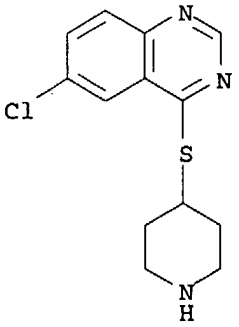
RN 232618-31-4 HCAPLUS
CN Quinazoline, 4-(4-piperidinylthio)- (9CI) (CA INDEX NAME)



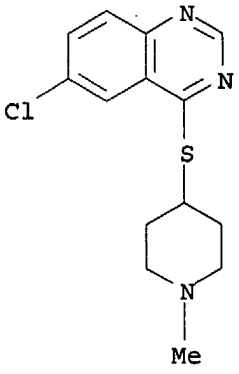
RN 232618-36-9 HCAPLUS
CN Quinazoline, 4-[(1-methyl-4-piperidinyl)thio]- (9CI) (CA INDEX NAME)



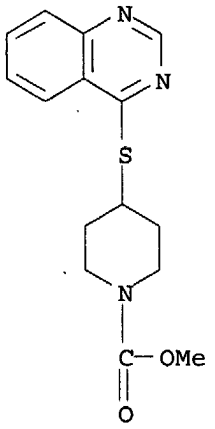
RN 325145-97-9 HCAPLUS
CN Quinazoline, 6-chloro-4-(4-piperidinylthio)- (9CI) (CA INDEX NAME)



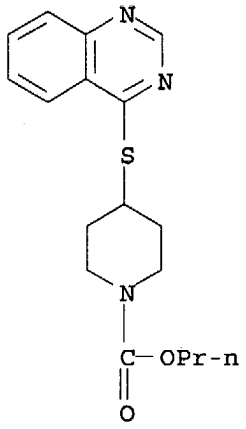
RN 325145-98-0 HCAPLUS
CN Quinazoline, 6-chloro-4-[(1-methyl-4-piperidinyl)thio]- (9CI) (CA INDEX NAME)



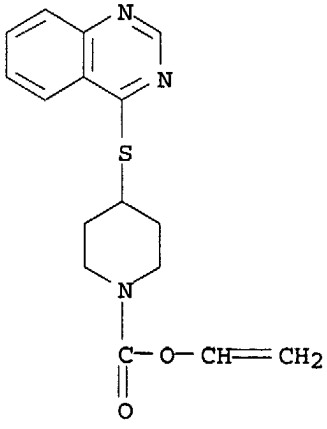
RN 325145-99-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, methyl ester (9CI) (CA INDEX NAME)



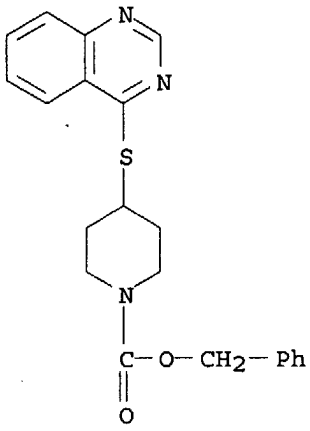
RN 325146-00-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, propyl ester (9CI) (CA INDEX NAME)



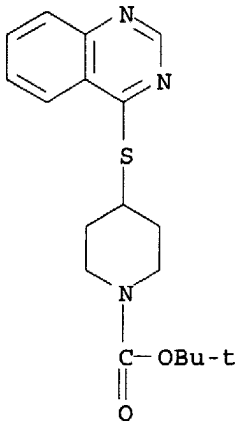
RN 325146-01-8 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, ethenyl ester (9CI) (CA INDEX NAME)



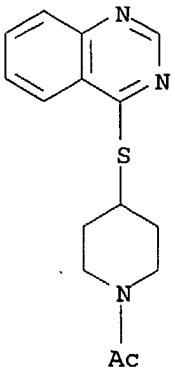
RN 325146-02-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, phenylmethyl ester (9CI) (CA INDEX NAME)



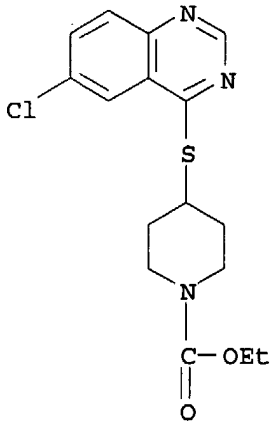
RN 325146-03-0 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



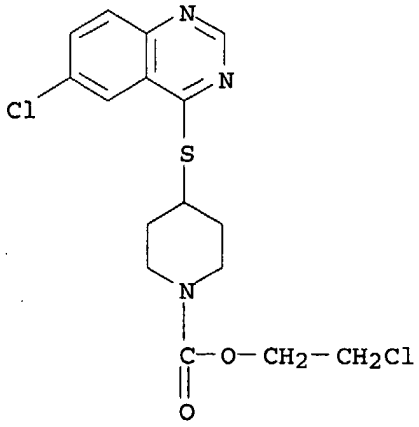
RN 325146-04-1 HCAPLUS
CN Piperidine, 1-acetyl-4-(4-quinazolinylthio)- (9CI) (CA INDEX NAME)



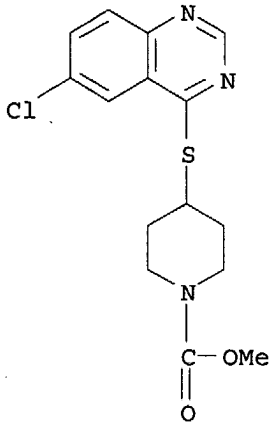
RN 325146-05-2 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, ethyl ester (9CI) (CA INDEX NAME)



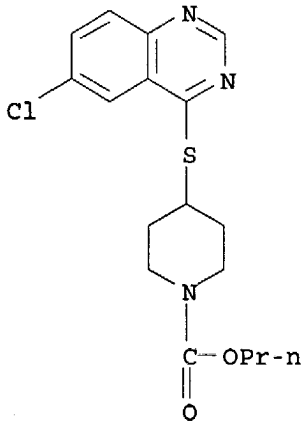
RN 325146-06-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, 2-chloroethyl ester (9CI) (CA INDEX NAME)



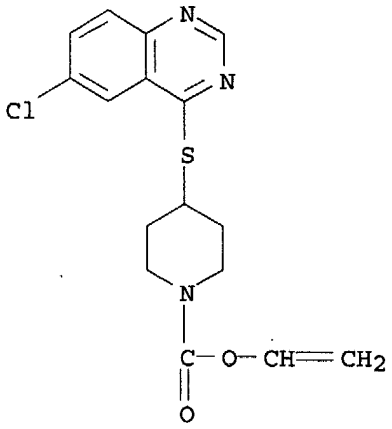
RN 325146-07-4 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, methyl ester (9CI) (CA INDEX NAME)



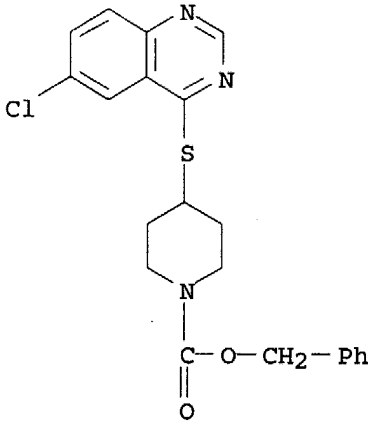
RN 325146-08-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, propyl ester (9CI) (CA INDEX NAME)



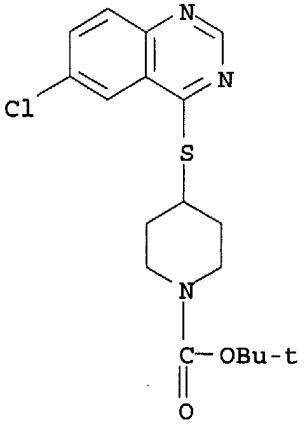
RN 325146-09-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, ethenyl ester (9CI) (CA INDEX NAME)



RN 325146-10-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 325146-11-0 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(6-chloro-4-quinazolinyl)thio]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

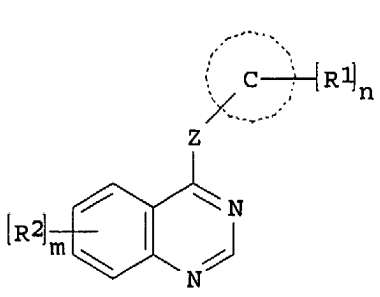


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

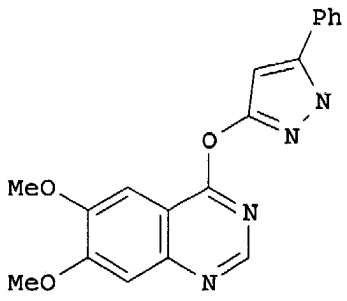
L40 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:260277 HCAPLUS
DOCUMENT NUMBER: 132:293771
TITLE: Preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors
INVENTOR(S): Hennequin, Laurent Francois Andre; Pasquet, Georges
PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma S.A.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021955	A1	20000420	WO 1999-GB3295	19991005
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344290	AA	20000420	CA 1999-2344290	19991005
AU 9961128	A1	20000501	AU 1999-61128	19991005
AU 756556	B2	20030116		
BR 9914326	A	20010626	BR 1999-14326	19991005
EP 1119567	A1	20010801	EP 1999-947758	19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527436	T2	20020827	JP 2000-575861	19991005
NZ 510434	A	20031031	NZ 1999-510434	19991005
ZA 2001002655	A	20020930	ZA 2001-2655	20010330
NO 2001001739	A	20010607	NO 2001-1739	20010406
PRIORITY APPLN. INFO.:			EP 1998-402496 A	19981008
			WO 1999-GB3295 W	19991005

OTHER SOURCE(S): MARPAT 132:293771
GI



I

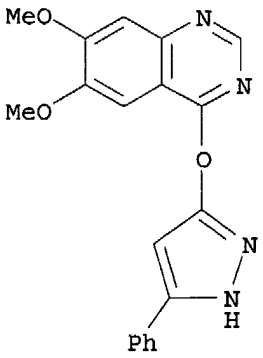


II

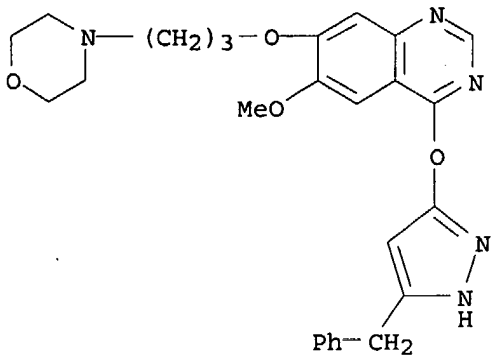
AB The title compds. [I; ring C = 5-6 membered heterocyclic moiety; Z = O, NH, S, CH2; R1 = H, alkyl, alkoxymethyl, etc.; n = 0-5; m = 0-3; R2 = H, OH, halo, etc.] and their salts which inhibit the effects of VEGF , and therefore useful in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals, were prepared and formulated. E.g., a multi-step synthesis of quinazoline II was given. Compds. I are effective at 1-50 mg/kg/day.

IT **264207-46-7P 264207-48-9P 264207-50-3P**
264207-52-5P 264207-54-7P 264207-56-9P
264207-58-1P 264207-60-5P 264207-62-7P
264207-64-9P 264207-66-1P 264207-68-3P
264207-70-7P 264207-72-9P 264207-74-1P
264207-76-3P 264207-94-5P 264207-96-7P
264207-98-9P 264208-00-6P 264208-02-8P
264208-04-0P 264208-06-2P 264208-08-4P
264208-10-8P 264208-12-0P 264208-14-2P
264208-16-4P 264208-18-6P 264208-21-1P
264208-23-3P 264208-26-6P 264208-28-8P
264208-31-3P 264208-33-5P 264208-35-7P
264208-38-0P 264208-41-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of quinazolines as VEGF receptor tyrosine kinase inhibitors)

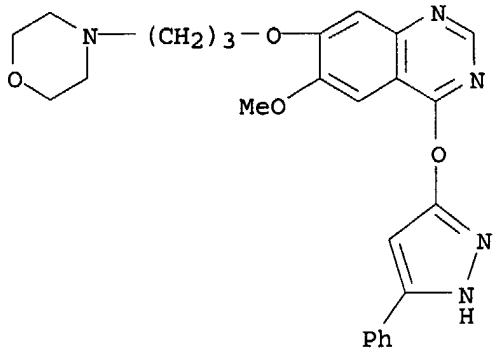
RN 264207-46-7 HCAPLUS
CN Quinazoline, 6,7-dimethoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



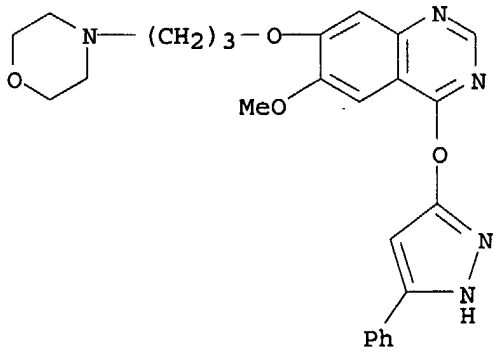
RN 264207-48-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(phenylmethyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



RN 264207-50-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

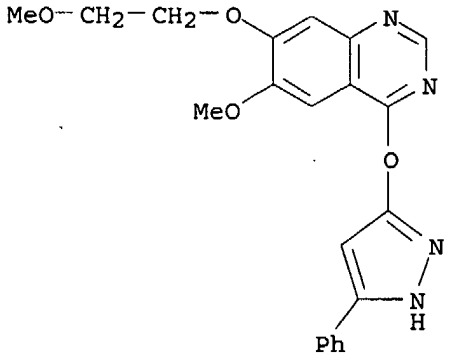


RN 264207-52-5 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, dihydrochloride (9CI) (CA INDEX NAME)

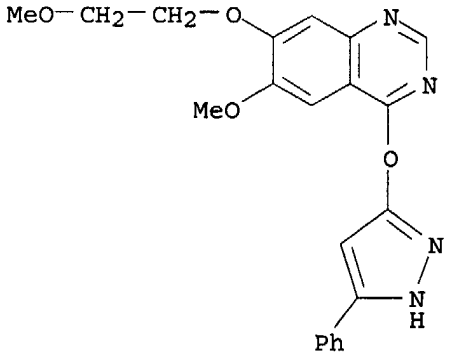


●2 HCl

RN 264207-54-7 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

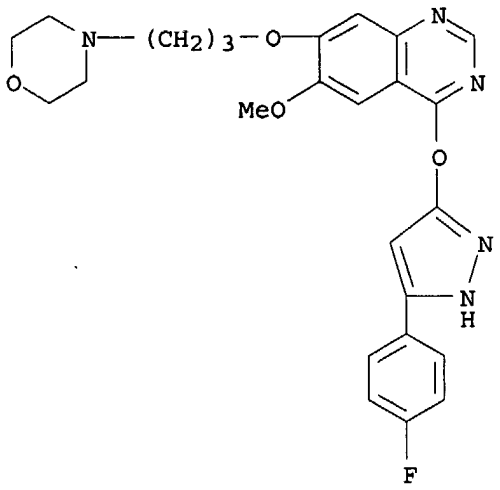


RN 264207-56-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (4:3) (9CI) (CA INDEX NAME)



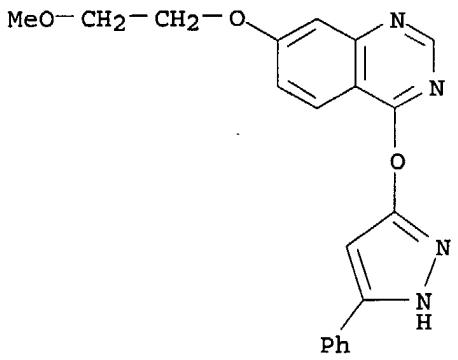
●3/4 HCl

RN 264207-58-1 HCAPLUS
CN Quinazoline, 4-[[5-(4-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)



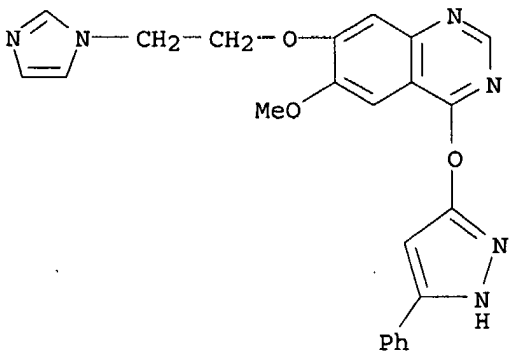
●19/10 HCl

RN 264207-60-5 HCAPLUS
CN Quinazoline, 7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (5:3) (9CI) (CA INDEX NAME)



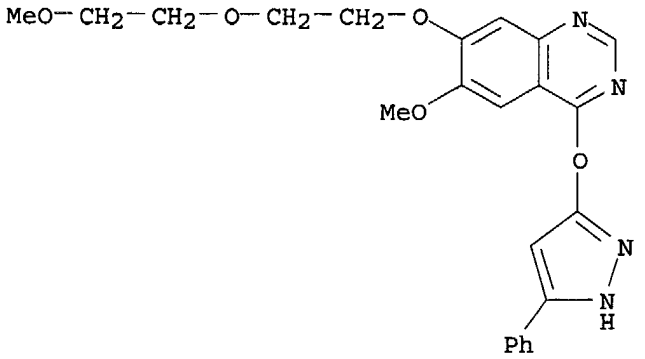
●3/5 HCl

RN 264207-62-7 HCAPLUS
CN Quinazoline, 7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (2:5) (9CI) (CA INDEX NAME)



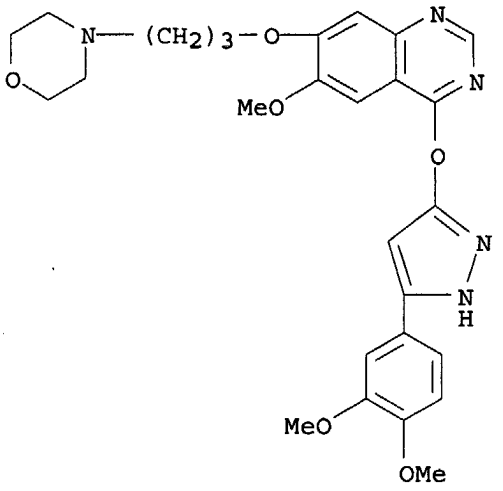
●5/2 HCl

RN 264207-64-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]-, hydrochloride (20:17) (9CI) (CA INDEX NAME)

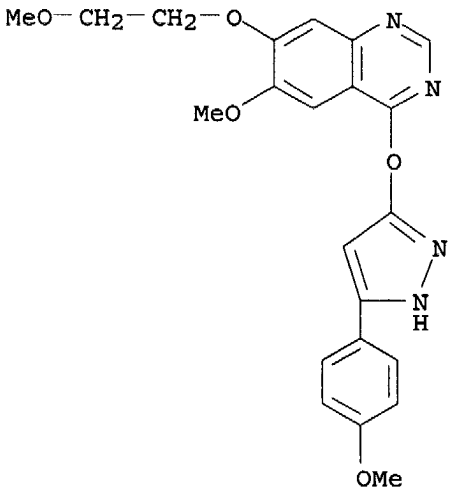


●17/20 HCl

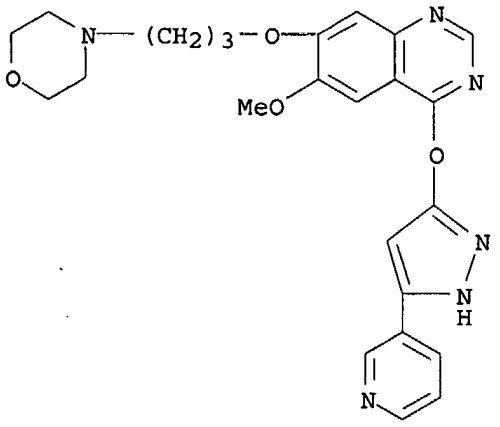
RN 264207-66-1 HCAPLUS
CN Quinazoline, 4-[[5-(3,4-dimethoxyphenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



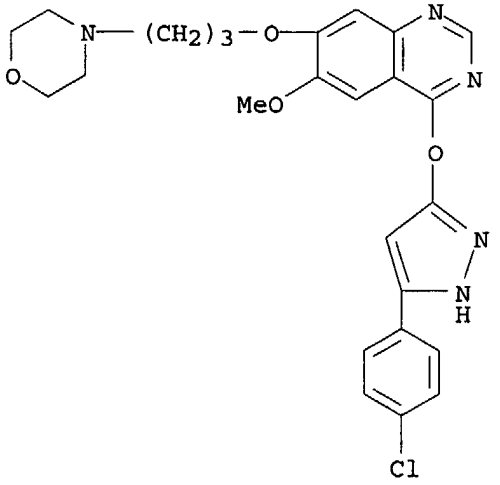
RN 264207-68-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-(2-methoxyethoxy)-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



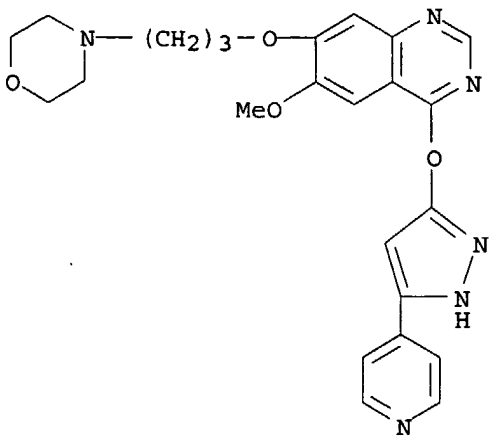
RN 264207-70-7 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(3-pyridinyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



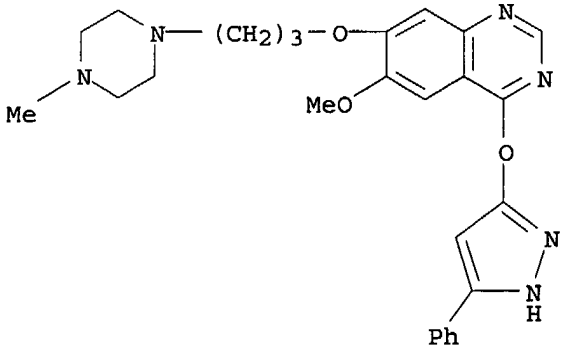
RN 264207-72-9 HCAPLUS
CN Quinazoline, 4-[[5-(4-chlorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



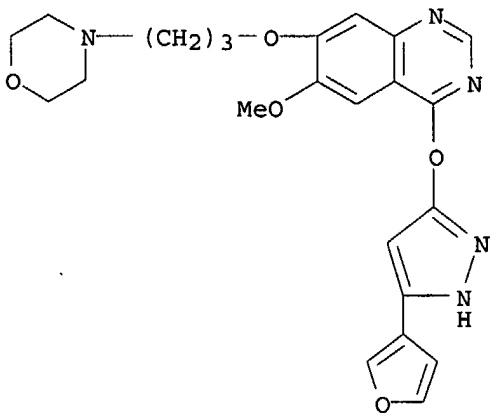
RN 264207-74-1 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(4-pyridinyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



RN 264207-76-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

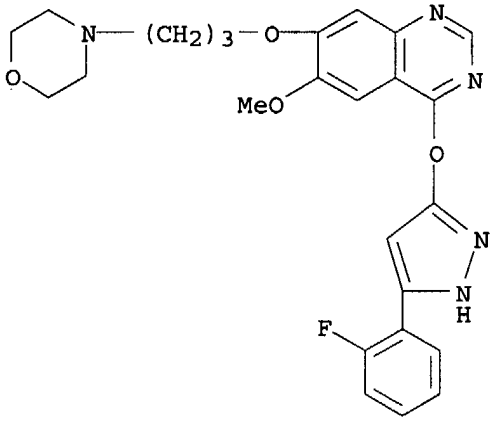


RN 264207-94-5 HCAPLUS
CN Quinazoline, 4-[[5-(3-furanyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]-, hydrochloride (9CI) (CA INDEX NAME)

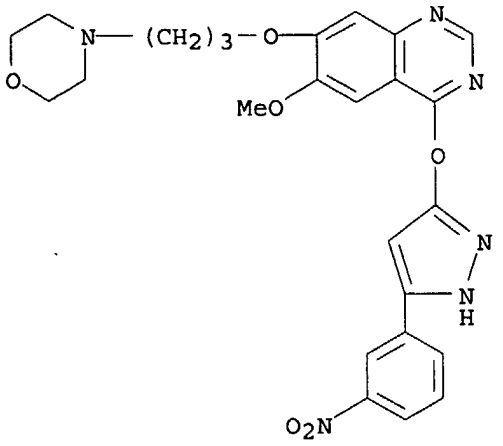


●x HCl

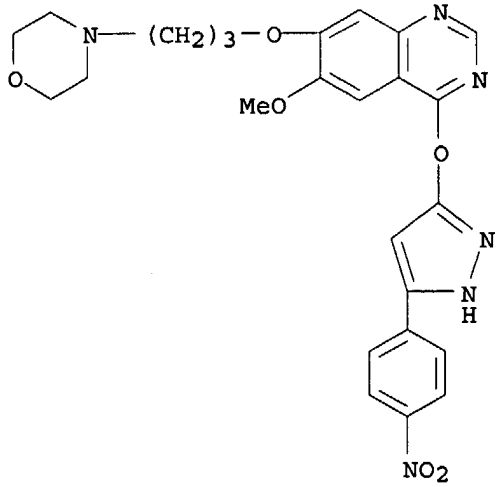
RN 264207-96-7 HCAPLUS
CN Quinazoline, 4-[[5-(2-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



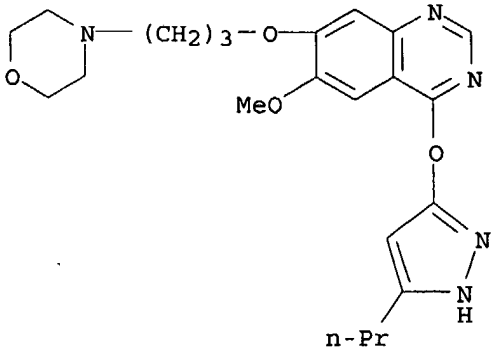
RN 264207-98-9 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(3-nitrophenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



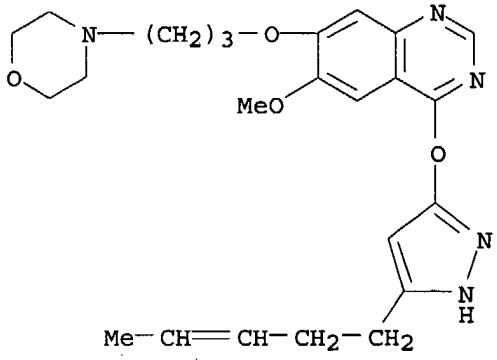
RN 264208-00-6 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(4-nitrophenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



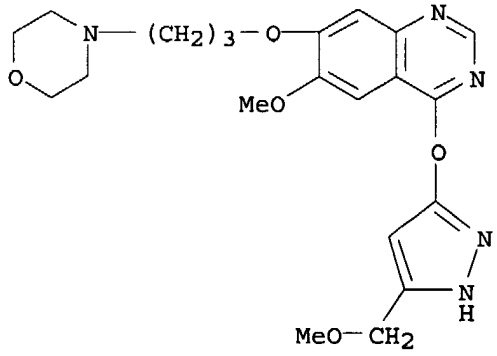
RN 264208-02-8 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[(5-propyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



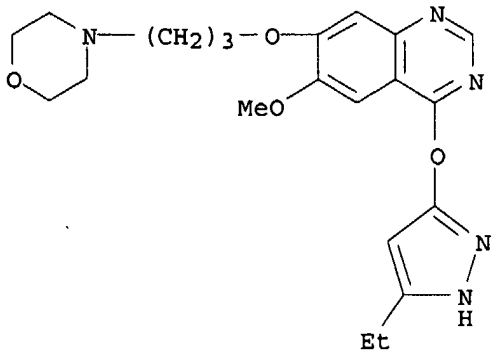
RN 264208-04-0 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(3-pentenyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



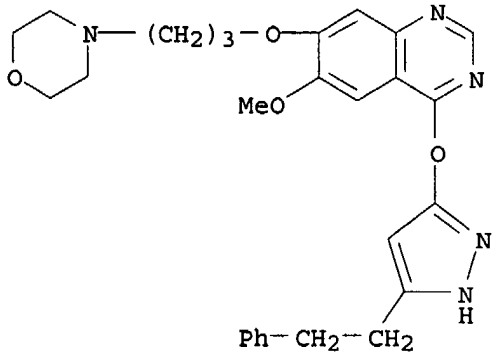
RN 264208-06-2 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(methoxymethyl)-1H-pyrazol-3-yl]oxy]-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



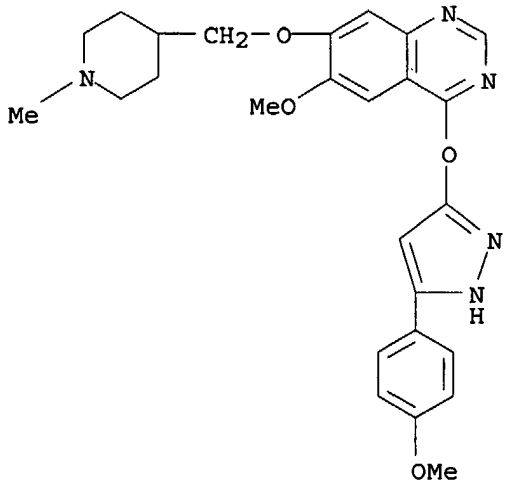
RN 264208-08-4 HCAPLUS
CN Quinazoline, 4-[(5-ethyl-1H-pyrazol-3-yl)oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



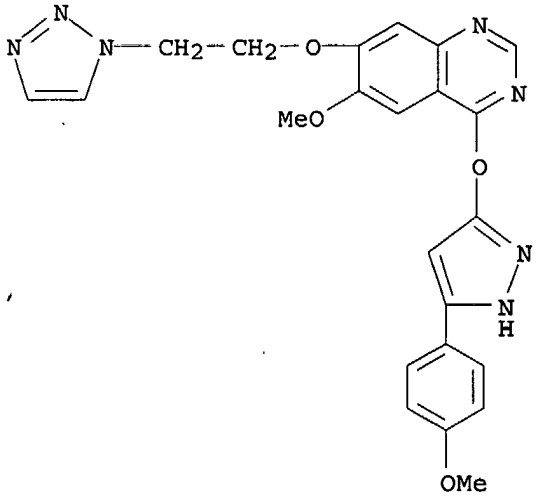
RN 264208-10-8 HCAPLUS
CN Quinazoline, 6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-[[5-(2-phenylethyl)-1H-pyrazol-3-yl]oxy]- (9CI) (CA INDEX NAME)



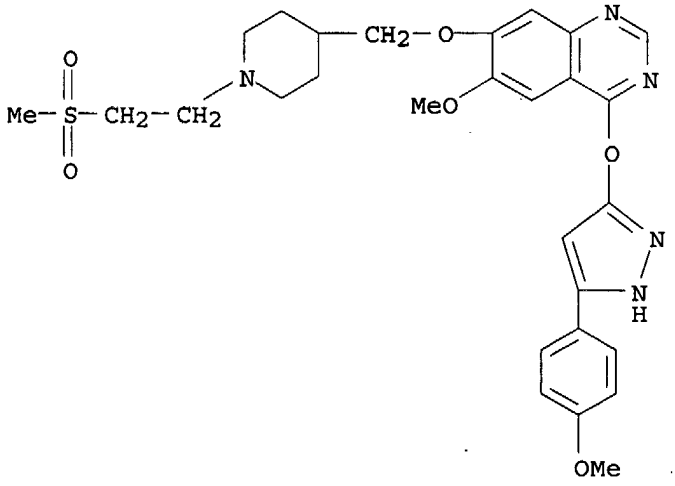
RN 264208-12-0 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[(1-methyl-4-piperidinyl)methoxy]- (9CI) (CA INDEX NAME)



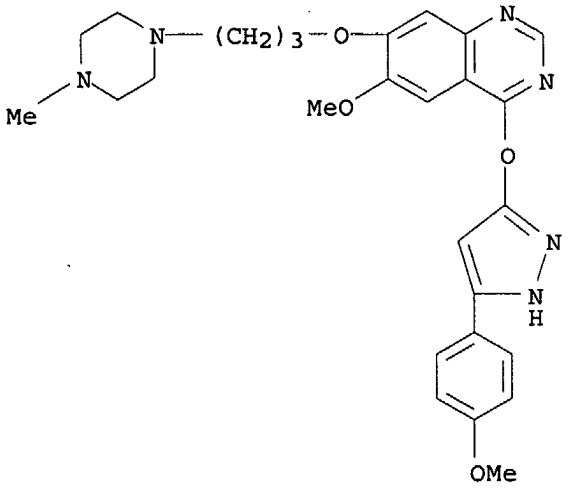
RN 264208-14-2 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]- (9CI) (CA INDEX NAME)



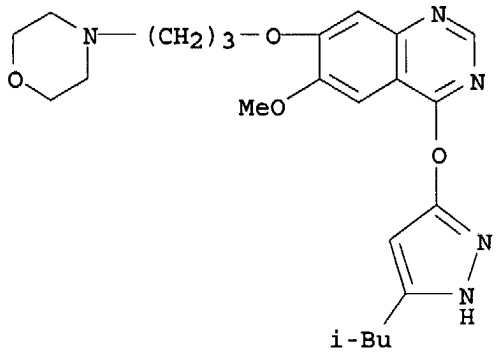
RN 264208-16-4 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[[1-[2-(methylsulfonyl)ethyl]-4-piperidinyl]methoxy]- (9CI) (CA INDEX NAME)



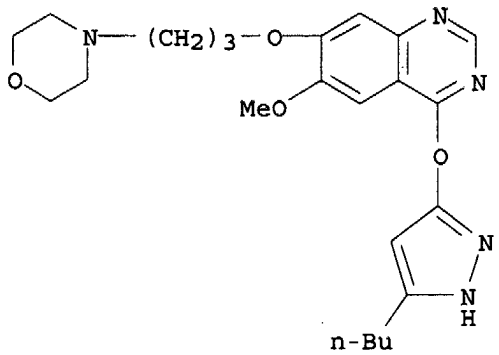
RN 264208-18-6 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



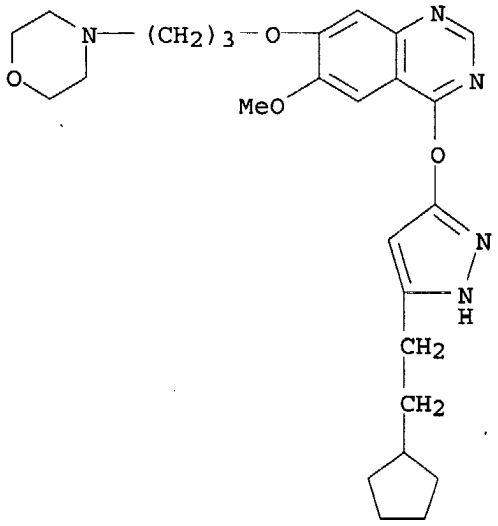
RN 264208-21-1 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(2-methylpropyl)-1H-pyrazol-3-yl]oxy]-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



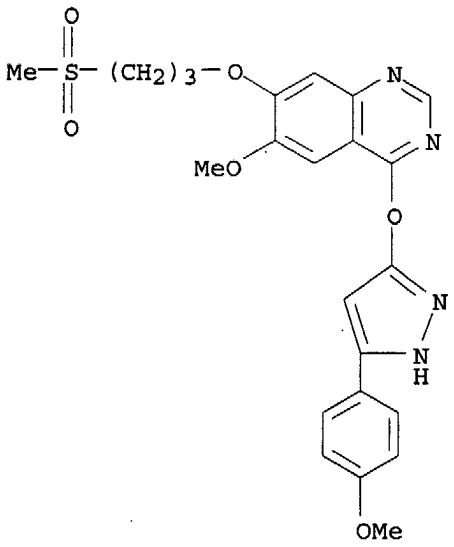
RN 264208-23-3 HCAPLUS
CN Quinazoline, 4-[(5-butyl-1H-pyrazol-3-yl)oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



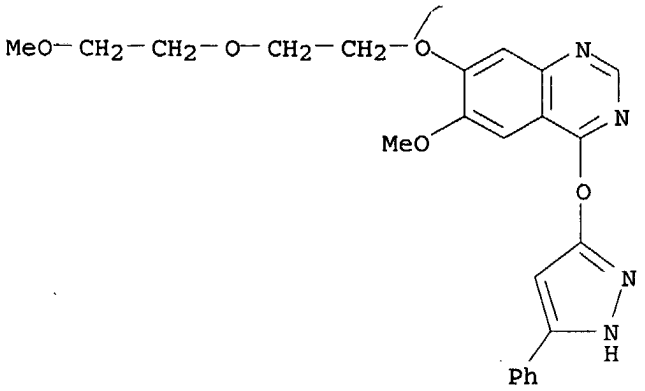
RN 264208-26-6 HCAPLUS
CN Quinazoline, 4-[[5-(2-cyclopentylethyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



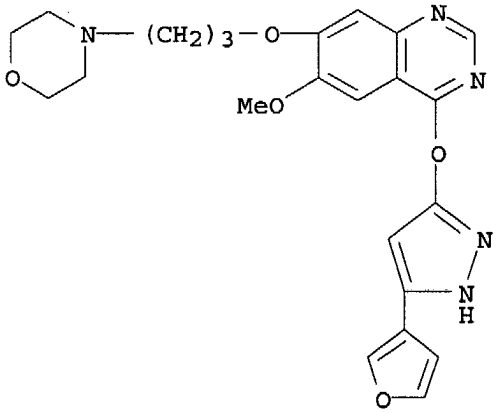
RN 264208-28-8 HCAPLUS
CN Quinazoline, 6-methoxy-4-[[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]oxy]-7-[3-(methylsulfonyl)propoxy]- (9CI) (CA INDEX NAME)



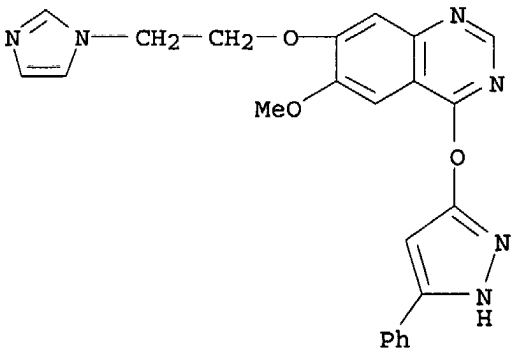
RN 264208-31-3 HCAPLUS
CN Quinazoline, 6-methoxy-7-[2-(2-methoxyethoxy)ethoxy]-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)



RN 264208-33-5 HCAPLUS
CN Quinazoline, 4-[[5-(3-furanyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)

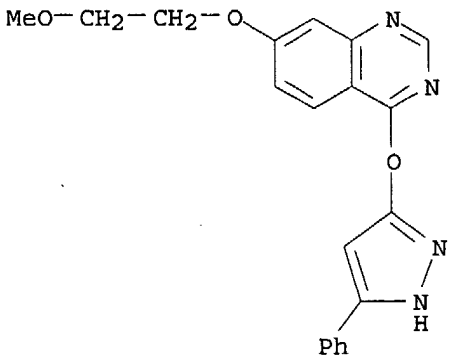


RN 264208-35-7 HCAPLUS
CN Quinazoline, 7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI) (CA INDEX NAME)

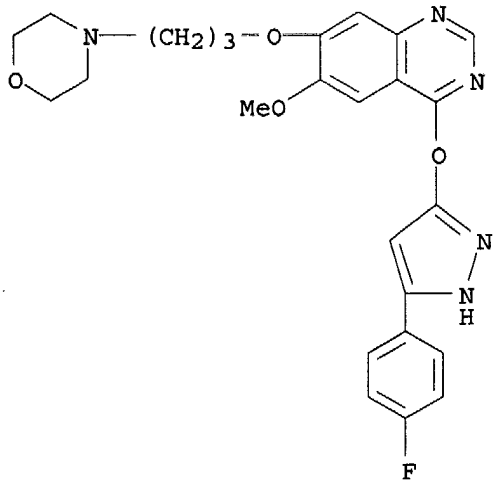


RN 264208-38-0 HCAPLUS
CN Quinazoline, 7-(2-methoxyethoxy)-4-[(5-phenyl-1H-pyrazol-3-yl)oxy]- (9CI)

(CA INDEX NAME)



RN 264208-41-5 HCAPLUS
CN Quinazoline, 4-[[5-(4-fluorophenyl)-1H-pyrazol-3-yl]oxy]-6-methoxy-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



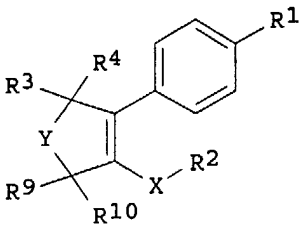
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:83114 HCAPLUS
DOCUMENT NUMBER: 132:122509
TITLE: Preparation of (methylsulfonyl)phenyl-2-(5H)-furanones as COX-2 inhibitors
INVENTOR(S): Belley, Michel; Gauthier, Jacques Yves; Grimm, Erich; Leblanc, Yves; Li, Chun-sing; Therien, Michel; Black, Cameron; Prasit, Petpiboon; Lau, Cheuk-kun; Roy, Patrick
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: U.S., 88 pp., Cont.-in-part of U.S. Ser. No. 728,512, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6020343	A	20000201	US 1998-97543		19980615
NZ 332820	A	20000526	NZ 1996-332820		19961009
JP 2001199954	A2	20010724	JP 2000-366579		19961009
ZA 9608609	A	19970414	ZA 1996-8609		19961011
US 6169188	B1	20010102	US 1999-422151		19991021
PRIORITY APPLN. INFO.:			US 1995-5371P	P	19951013
			US 1996-11637P	P	19960214
			US 1996-728512	B2	19961009
			GB 1996-2939	A	19960213
			GB 1996-5645	A	19960318
			JP 1997-515371	A3	19961009
			NZ 1996-319090	A1	19961009
			US 1998-97543	A3	19980615

OTHER SOURCE(S): MARPAT 132:122509
GI



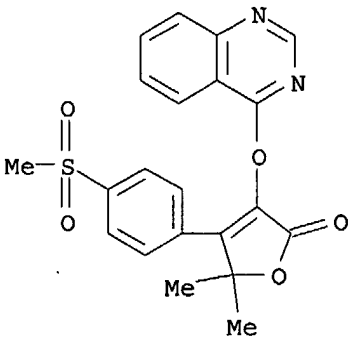
I

AB The title compds. [I; X = CH2, CHOH, CO, etc.; Y = O, S, CO, etc.; R1 = SO2Me, SO2NHCOCF3, SONHNH2, etc.; R2 = alkyl, (un)substituted Ph, naphthyl, etc.; R3 = H, alkyl, CN, etc.; R4 = H, alkyl, alkoxy, etc.; R9, R10 = H, alkyl; R9 and R10 together with the carbon atom to which they are attached form a carbonyl or thiocarbonyl group], useful in the treatment of cyclooxygenase-2 mediated diseases such as inflammation, arthritis, osteoporosis, rheumatoid arthritis, and pain, were prepared E.g., a 4-step synthesis of I [X = O; Y = O; R1 = SO2Me; R2 = 3,4-F2C6H3; R3 = R4 = Me; R9 and R10 together with the carbon atom to which they are attached form a carbonyl group] which showed ED50 of 0.14 mg/kg in rat paw edema assay, was given.

IT **189955-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of (methylsulfonyl)phenyl-2-(5H)-furanones as COX-2 inhibitors)

RN 189955-00-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



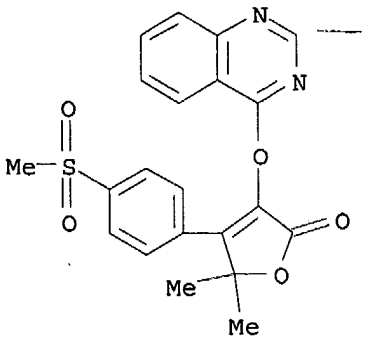
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:769077 HCAPLUS
DOCUMENT NUMBER: 132:73232
TITLE: Synthesis and biological evaluation of 3-heteroaryloxy-4-phenyl-2(5H)-furanones as selective COX-2 inhibitors
AUTHOR(S): Lau, Cheuk K.; Brideau, Christine; Chan, Chi Chung; Charleson, Stella; Cromlish, Wanda A.; Ethier, Diane; Gauthier, Jacques Yves; Gordon, Robert; Guay, Jocelyne; Kargman, Stacia; Li, Chun-Sing; Prasit, Petpiboon; Riendeau, Denis; Therien, Michel; Visco, Denise M.; Xu, Lijing
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(22), 3187-3192
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of 3-heteroaryloxy-4-phenyl-2-(5H)-furanones were prepared and evaluated for their potency and selectivity as COX-2 inhibitors. This led to the identification of L-778,736 as a potent, orally active and selective inhibitor of the COX-2 enzyme.

IT **189955-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and structure-anti-inflammatory activity of cyclooxygenase 2 inhibitors heteroaryloxyphenylfuranones)

RN 189955-00-8 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)

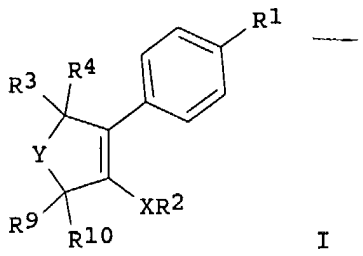


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:718982 HCAPLUS
DOCUMENT NUMBER: 131:322532
TITLE: Preparation of 4-aryl-(5H)-furan-2-ones as cyclooxygenase-2 inhibitors.
INVENTOR(S): Belley, Michel; Gauthier, Jacques Yves; Grimm, Erich; Leblanc, Yves; Li, Chun-Sing; Therien, Michel; Black, Cameron; Prasit, Petpiboon; Lau, Cheuk-Kun; Roy, Patrick
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 728,512, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5981576	A	19991109	US 1998-97537		19980615
NZ 332820	A	20000526	NZ 1996-332820		19961009
JP 2001199954	A2	20010724	JP 2000-366579		19961009
ZA 9608609	A	19970414	ZA 1996-8609		19961011
PRIORITY APPLN. INFO.:			US 1995-5371P	P	19951013
			US 1996-11637P	P	19960214
			US 1996-728512	B2	19961009
			GB 1996-2939	A	19960213
			GB 1996-5645	A	19960318
			JP 1997-515371	A3	19961009
			NZ 1996-319090	A1	19961009

OTHER SOURCE(S): MARPAT 131:322532
GI



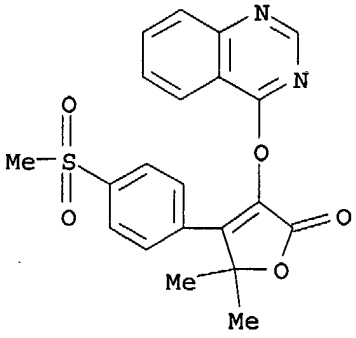
I

AB Title compds. [I; X = CH2, CH(OH), CO, O, S, NR15; Y = CO, O, S, CR11R12; R1 = SO2Me, SO2NR16R17, SO2NHCOCF3, etc.; R2 = alkyl, (substituted) Ph, naphthyl, heteroaryl, benzoheterocyclyl, heterocyclylalkyl, benzocarbocyclyl, etc.; R3 = H, alkyl, CH2OR7, cyano, CH2CN, (substituted) Ph, etc.; R4 = H, alkyl, alkoxy, alkylthio, OH, SH, OCOR7, etc.; R3R4 = atoms to form a 3-7 membered ring; R7 = H, alkyl, (substituted) Ph, PhCH2; R9, R10 = H, alkyl; R9R10 = O, S; R16, R17 = H, alkyl, alkanoic acid, alkyl amine, etc.; with provisos], were prepared Thus, cyclopropanemethanol in THF was added to NaH in THF at 12° over 75 min. followed by 18 h stirring at room temperature; ClCH2CO2Na was added followed by 8.5 h reflux to give an oil. This was refluxed with 2-bromo-2-methyl-1-[(4-methylsulfonyl)phenyl]propan-1-one (preparation given) and ethyldiisopropylamine in EtOH to give cyclopropylmethoxyacetic acid 2-methyl-1-[(4-methylsulfonyl)phenyl]propan-1-one ester. The latter was refluxed with iso-Pr trifluoroacetate and DBU in MeCN to give 3-(cyclopropylmethoxy)-5,5-dimethyl-4-[(4-methylsulfonyl)phenyl]-5H-furan-2-one. I inhibited rat paw edema with ED50 = 0.32-10 mg/kg orally.

IT **189955-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of 4-aryl-(5H)-furan-2-ones as cyclooxygenase-2 inhibitors)

RN 189955-00-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

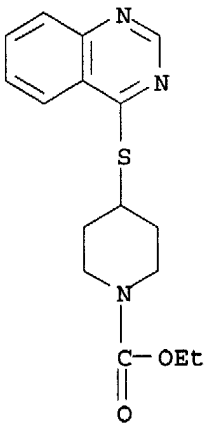
L40 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:410148 HCAPLUS
DOCUMENT NUMBER: 131:111116

TITLE: Synthesis and analgesic activity of some condensed analogs of anpirtoline
AUTHOR(S): Radl, Stanislav; Kovarova, Lenka; Hezky, Petr; Vosatka, Vaclav; Konigova, Otylie; Proska, Jan; Krejci, Ivan
CORPORATE SOURCE: Research Institute Pharmacy Biochemistry, Prague, 13060, Czech Rep.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1999), 332(6), 208-212
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Condensed derivs. of anpirtoline, in which the pyridine ring is replaced with quinoline, isoquinoline, quinazoline, and phthalazine nuclei, were synthesized. Their receptor binding profiles (5HT1A, 5-HT1B) and analgesic activity (hot plate, AcOH-induced writhing) were studied. The analgesic activity of 4 of the compds. are at least comparable to that of the clin. used drugs flupirtine and tramadol under the same conditions.

IT **232618-27-8P 232618-32-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation and 5-HT1-agonistic and analgesic activity of condensed analogs of anpirtoline)

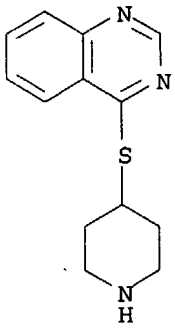
RN 232618-27-8 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-quinazolinylthio)-, ethyl ester (9CI) (CA INDEX NAME)



RN 232618-32-5 HCAPLUS
CN Quinazoline, 4-(4-piperidinylthio)-, monoacetate (9CI) (CA INDEX NAME)

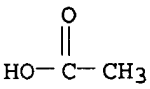
CM 1

CRN 232618-31-4
CMF C13 H15 N3 S

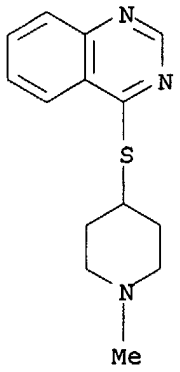


CM 2

CRN 64-19-7
CMF C2 H4 O2



IT **232618-36-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and 5-HT1-agonistic and analgesic activity of condensed analogs of anpirtoline)
RN 232618-36-9 HCAPLUS
CN Quinazoline, 4-[(1-methyl-4-piperidinyl)thio]- (9CI) (CA INDEX NAME)



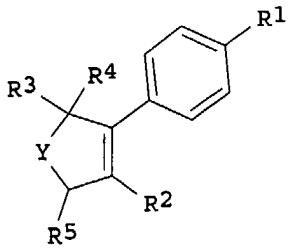
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:425272 HCAPLUS
DOCUMENT NUMBER: 127:34112
TITLE: Preparation of 3,4-diaryl-2-hydroxy-2,5-dihydrofurans as prodrugs to cyclooxygenase-2 (cox-2) inhibitors and as non-steroidal anti-inflammatory agents

INVENTOR(S): Black, Cameron; Leger, Serge; Prasit, Petpiboon; Wang, Zhaoyin; Hamel, Pierre; Han, Yongxin; Hughes, Gregory
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.
SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9716435	A1	19970509	WO 1996-CA717		19961029
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
US 5698584	A	19971216	US 1996-738143		19961025
CA 2234642	AA	19970509	CA 1996-2234642		19961029
AU 9672736	A1	19970522	AU 1996-72736		19961029
AU 711902	B2	19991021			
JP 11500748	T2	19990119	JP 1996-516943		19961029
EP 904269	A1	19990331	EP 1996-934267		19961029
EP 904269	B1	20020123			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, LI, LU, NL, SE, PT, IE, FI					
AT 212343	E	20020215	AT 1996-934267		19961029
ES 2171723	T3	20020916	ES 1996-934267		19961029
JP 3337477	B2	20021021	JP 1997-516943		19961029
US 6057319	A	20000502	US 1998-68139		19981002
PRIORITY APPLN. INFO.:			US 1995-8074P	P	19951030
			GB 1996-2877	A	19960213
			WO 1996-CA717	W	19961029

OTHER SOURCE(S): MARPAT 127:34112
GI



I

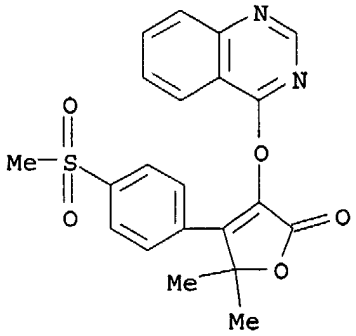
AB The invention encompasses the novel compound of formula [I; Y = (un)substituted CH2, O, S, CO; R2 = SO2Me, (un)substituted SO2NH2, SO2NHCOCF3, SONHNH2, SONHNHCOCF3, P(O)MeNH2, P(O)Me2, C(S)NH2; R2 = NR10R11, SR11, OR11, R11, C1-10 alkenyl, C1-10 alkynyl, (un)substituted C3-10 cycloalkenyl; wherein R11 = C1-10 alkyl, C3-10 cycloalkyl, (un)substituted Ph, naphthyl, or heteroaryl, etc.; R3 = H, C1-10 alkyl, cyano, CH2CN, C1-6 fluoroalkyl, F, CH2OR8, CON(R8)2; R4 = H, C1-10 alkyl, C1-10 alkoxy, C1-10 alkylthio, OH, O2CR8, SH, SCOR8, OCO2R8, O CON(R8)2,

SCON(R8)2, C3-10 cycloalkoxy or cycloalkylthio; or CR3R4 = 3- to 7-membered monocyclic ring optionally containing 1 or 2 heteroatoms selected from O, S, or N; wherein R8 = H, C1-10 alkyl, C1-10 alkyl-CO2H, C1-10 aminoalkyl, (un)substituted Ph or CH2Ph, C3-10 cycloalkyl, C1-10 alkanoyl, (un)substituted benzoyl; R5 = OR17, SR18, NR17R18, S(O)R18, SO2 R18, SO2N(R17)2, OP(O)(OR16)2; wherein R16 = H, C1-6 alkyl, (un)substituted CH2Ph; R17 = H, R18; R18 = C1-10 alkyl, C1-10 alkyl-CO2H, C1-10 aminoalkyl, (un)substituted Ph or CH2Ph, C3-10 cycloalkyl, (CH2CH2O)nH (n = 1-6), C1-10 alkanoyl, (un)substituted benzoyl]. They are in vivo converted into the active lactone form, i.e. arylhydroxydihydrofuranone derivs. I (R5 = oxo; Y, R1 - R4 = same as above) with high inhibitory activity against cyclooxygenase-2 and/or a specificity for cyclooxygenase-2 over cyclooxygenase-1 and useful in the treatment of cyclooxygenase-2 mediated diseases, in particular inflammatory diseases. Thus, 3,4-difluorophenoxyacetic acid was cyclocondensed with 2-hydroxy-4'-(methylsulfonyl)isobutyrophenone (preparation given) using 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-p-toluenesulfonate and 4-dimethylaminopyridine in CH2Cl2 at room temperature for 18 h to give 3-(3,4-difluorophenoxy)-5,5-dimethyl-4-(4-methylsulfonylphenyl)-5H-furan-2-one, which was reduced by (Me2CHCH2)2AlH in THF at room temperature for 30 min to give I (Y = O, R2 = 3,4-difluorophenoxy, R3 = R4 = Me, R5 = OH). The latter compound showed ED50 of 0.09 mg/kg p.o. for inhibiting the carrageenan-induced paw edema in rats.

IT **189955-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of diarylhydroxydihydrofurans as prodrugs for antiinflammatory diarylhydroxydihydrofuranones and selective cyclooxygenase-2 inhibitors)

RN 189955-00-8 HCAPLUS

CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



L40 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:384238 HCAPLUS

DOCUMENT NUMBER: 127:5002

TITLE: (Methylsulfonyl)phenyl-2-(5H)-furanones as cox-2 inhibitors

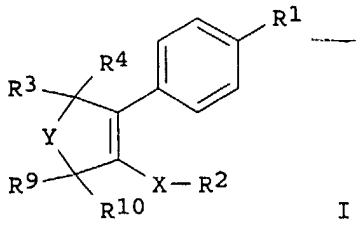
INVENTOR(S): Belley, Michel; Gauthier, Jacques Y.; Grimm, Erich; Leblanc, Yves; Li, Chung-Sing; Therien, Michel; Black, Cameron; Lau, Cheuk-Kun; Prasit, Petpiboon; et al.

PATENT ASSIGNEE(S): Can.
SOURCE: PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714691	A1	19970424	WO 1996-CA682	19961009
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HR 960458	B1	20030831	HR 1996-960458	19961007
CA 2233178	AA	19970424	CA 1996-2233178	19961009
CA 2233178	C	20031223		
AU 9671236	A1	19970507	AU 1996-71236	19961009
AU 703871	B2	19990401		
EP 863891	A1	19980916	EP 1996-932417	19961009
EP 863891	B1	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
CN 1200119	A	19981125	CN 1996-197609	19961009
JP 11500146	T2	19990106	JP 1997-515371	19961009
JP 3337476	B2	20021021		
BR 9611015	A	19990914	BR 1996-11015	19961009
NZ 319090	A	20000128	NZ 1996-319090	19961009
NZ 332820	A	20000526	NZ 1996-332820	19961009
JP 2001199954	A2	20010724	JP 2000-366579	19961009
IL 123699	A1	20020310	IL 1996-123699	19961009
SK 282639	B6	20021008	SK 1998-450	19961009
AT 229515	E	20021215	AT 1996-932417	19961009
EE 3969	B1	20030217	EE 1998-80	19961009
PT 863891	T	20030331	PT 1996-932417	19961009
ES 2187675	T3	20030616	ES 1996-932417	19961009
ZA 9608609	A	19970414	ZA 1996-8609	19961011
TW 426679	B	20010321	TW 1996-85112463	19961012
NO 9801628	A	19980527	NO 1998-1628	19980408
BG 63391	B1	20011231	BG 1998-102425	19980504

PRIORITY APPLN. INFO.:		
US 1995-5371P	P	19951013
GB 1996-2939	A	19960213
US 1996-11637P	P	19960214
GB 1996-5645	A	19960318
US 1995-5371	P	19951013
US 1996-11637	P	19960214
JP 1997-515371	A3	19961009
NZ 1996-319090	A1	19961009
WO 1996-CA682	W	19961009

OTHER SOURCE(S): MARPAT 127:5002
GI



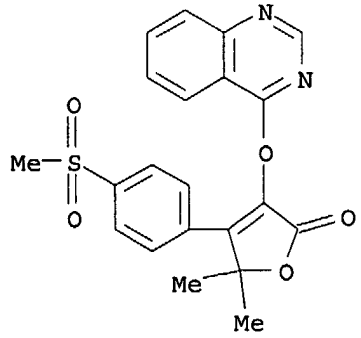
I

AB The title compds. [I; X = CH2, CHOH, CO, O, S, NR15 with the proviso that when R3 and R4 are other than both H, both C1-10 alkyl, or joined together with the carbon to which they are attached to form a saturated monocyclic carbon ring of 3, 4, 5, 6 or 7 atoms, then X is selected from CO, O, S, or NR15; Y = CR11R12, CO, O, S; R11, R12 = H, mono- or disubstituted Ph or mono- or disubstituted benzyl or mono- or disubstituted heteroaryl or mono- or disubstituted heteroarylmethyl wherein the substituents are H, halo, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, etc.; R1 = SO2-Me, SO2-NR16R17, SO2-NH-CO-CF3, SONH-NH2, etc.; R2 = H, halo, C1-10 alkyl, mono- or disubstituted Ph or naphthyl wherein the substituents are selected from the group consisting of H, halo, C1-10 alkoxy, C1-10 alkylthio, etc.; R3 = H, C1-10 alkyl, CH2-OR7, CN, CH2CN, C1-6 fluoroalkyl, F, etc.; R4 = H, C1-10 alkyl, C1-10 alkoxy, C1-10 alkylthio, OH, etc.; R9, R10 = H, C1-7 alkyl, or R9R10 together with the carbon atom they are attached form a carbonyl or thiocarbonyl group; R15 = H, C1-10 alkyl, mono-, di-, or trisubstituted Ph or naphthyl, etc.; R16, R17 = H, C1-10 alkyl, alkanoic acid, alkyl amine, etc.] are prepared Thus, 2-methyl-1-[4-(methylthio)phenyl]-1-propanone (prepared from isobutyryl chloride and thioanisole) was treated with Aliquat 336 to give the 2-hydroxy derivative, which was oxidized to the sulfonyl compound with Oxone, which was reacted with 3,4-difluorophenoxyacetic acid to give I [R1 = SO2-Me, R2 = 3,4-difluorophenyl, R3 = R4 = Me, R9R10 = O, X = Y = O]. In a red paw edema assay (using rats) for its antiinflammatory potency, this had ED50 of 0.14 mg/Kg. The invention also describes pharmaceutical compns. comprising I for treatment of cyclooxygenase-2 mediated diseases.

IT **189955-00-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
((methylsulfonyl)phenyl(5H)-furanones as cox-2 inhibitors)

RN 189955-00-8 HCAPLUS

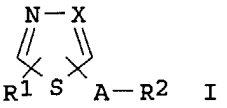
CN 2(5H)-Furanone, 5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-(4-quinazolinyloxy)- (9CI) (CA INDEX NAME)



L40 ANSWER 17 OF 24—HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:708170 HCAPLUS
DOCUMENT NUMBER: 125:328719
TITLE: Preparation of thiazoles and thiadiazoles for treatment of thrombocytopenia
INVENTOR(S): Matsuo, Masaaki; Ogino, Takashi; Tsuji, Kiyoshi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630370	A2	19961003	WO 1996-JP773	19960326
WO 9630370	A3	19961128		
W: AU, CA, CN, HU, JP, KR, NO, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9602398	A	19961001	ZA 1996-2398	19960326
AU 9650153	A1	19961016	AU 1996-50153	19960326
PRIORITY APPLN. INFO.:			GB 1995-6189 A	19950327
			GB 1995-11226 A	19950602
			WO 1996-JP773 W	19960326

OTHER SOURCE(S): MARPAT 125:328719
GI

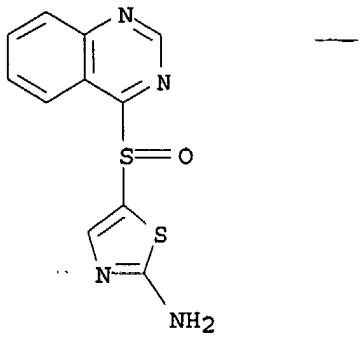


I

AB The title compds. [I; R1 = H, halo, NH2, etc.; R2 = N- or S-containing unsatd. heterocyclic group; X = CH, N; A = S(O)m (wherein m = 0-2)], useful for prophylactic or therapeutic treatment of thrombocytopenia, rheumatism, nephritis, tumor or side effects of antitumor agents, were prepared Thus, reaction of 2-amino-5-chlorothiazole.HCl with 2-quinolinethiol in the presence of NaHCO3 in DMF at 110° afforded I [R1 = 2-NH2; AR2 = 5-(2-quinolylthio)-; X = CH] which showed 74% increase in platelet number at 100 mg/kg in male ddY mice.

IT **183548-92-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of thiazoles and thiadiazoles for treatment of thrombocytopenia)

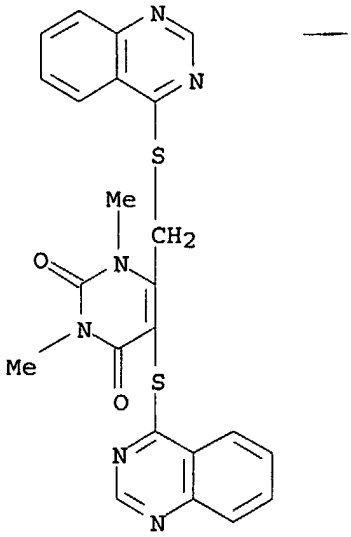
RN 183548-92-7 HCAPLUS
CN 2-Thiazolamine, 5-(4-quinazolinylsulfinyl)- (9CI) (CA INDEX NAME)



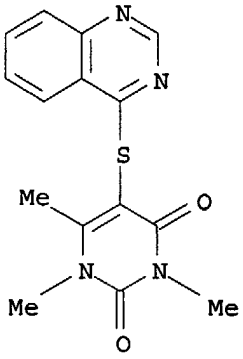
L40 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:731257 HCAPLUS
DOCUMENT NUMBER: 123:339501
TITLE: Reactions of diazines with nucleophiles. IV. The reactivity of 5-bromo-1,3,6-trimethyluracil with thiolate ions - substitution versus X-philic versus single electron transfer reactions
AUTHOR(S): Kumar, Subodh; Chimni, Swapandeep Singh; Cannoo, Deepika; Arora, Jasbir Singh
CORPORATE SOURCE: Department Chemistry, Guru Nanak Dev University, Amritsar, 143 005, India
SOURCE: Bioorganic & Medicinal Chemistry (1995), 3(7), 891-7
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reaction of 5-bromo-1,3,6-trimethyluracil with alkylthiolate (propane-1-, toluene-α-, allyl-, etc.) ions under phase transfer catalytic conditions follows nucleophilic substitution and X-philic (Br and S) elimination to give 5-alkylthio-1,3,6-trimethyluracils, 6-alkylthiomethyl-1,3-dimethyluracils and 1,3,6 -trimethyluracil. Reaction of 5-bromo-1,3,6-trimethyluracil with heteroarylthiolate ions (pyridine-2-, quinazoline-4-, uracil-2- and 4,6-dimethylpyrimidine-2-thiolate) gives only nucleophilic substitution products. However, arylthiolate (phenyl-, 4-chlorophenyl-, 2-aminophenyl-) ions follow a single electron transfer (SET) mechanism to give 5-arylthio-6-arylthiomethyl-1,3-dimethyluracils along with normal substitution products. 1,3,6-Trimethyluracil does not react with alkyl- or heteroaryl-thiolate ions but reacts with arylthiolate ions (SET) providing mainly 5-arylthio-1,3,6-trimethyluracils.

IT **170504-08-2P 170504-11-7P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(reactions of 5-bromo-1,3,6-trimethyluracil with thiolate ions)
RN 170504-08-2 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-dimethyl-5-(4-quinazolinylthio)-6-[(4-quinazolinylthio)methyl]- (9CI) (CA INDEX NAME)



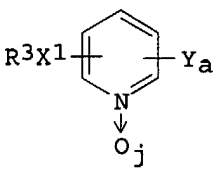
RN 170504-11-7 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3,6-trimethyl-5-(4-quinazolinylthio)- (9CI) (CA INDEX NAME)



L40 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:70632 HCAPLUS
DOCUMENT NUMBER: 108:70632
TITLE: Use of heterocyclic nitrogen-containing compounds for reducing moisture loss from plants and increasing crop yield
INVENTOR(S): Manning, David Treadway; Cappy, James Joseph; Cooke, Anson Richard; Sheads, Richard Eric; Wu, Tai Teh; Lopes, Anihal; Phillips, Jennifer Lyn; Outcalt, Russell James
PATENT ASSIGNEE(S): Union Carbide Agricultural Products Co., Inc., USA
SOURCE: PCT Int. Appl., 789 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8704321	A2	19870730	WO 1987-US240	19870123
WO 8704321	A3	19871105		
W: AU, BR, DK, FI, HU, JP, KR, LK, MW, NO, RO, SD, SU				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
DD 254318	A5	19880224	DD 1987-299404	19870122
ZA 8700480	A	19880928	ZA 1987-480	19870122
ES 2004071	A6	19881201	ES 1987-158	19870122
AU 8770316	A1	19870814	AU 1987-70316	19870123
EP 258391	A1	19880309	EP 1987-901826	19870123
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
BR 8705356	A	19880405	BR 1987-5356	19870123
JP 63502511	T2	19880922	JP 1987-501343	19870123
HU 45848	A2	19880928	HU 1987-1236	19870123
FI 8704111	A	19870921	FI 1987-4111	19870921
DK 8704961	A	19870922	DK 1987-4961	19870922
PRIORITY APPLN. INFO.:			US 1986-824389 A	19860123
			US 1986-939416 A	19861215
			WO 1987-US240 A	19870123

GI



I

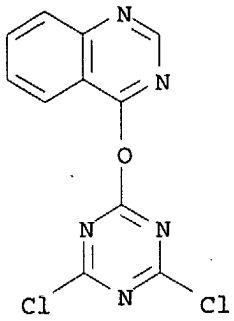
AB The title compds. R1XR2 [R1 = (un)substituted carbocyclic (aromatic or nonarom.) or heterocyclic ring; X = covalent single or double bond, (un)substituted heteroatom or substituted C, etc.; R2 = (un)substituted heterocyclic ring] are plant antitranspirants. The pyridines I [R3 = (un)substituted Ph, 1- or 2-naphthyl or heteroaryl; X1 = O, S, SO2, NH, CH2O, CH2S, etc.; Y = halo, alkyl, CN, polyhaloalkyl, alkoxy, etc.; a = 2-4, j = 0, 1] are novel compds. A solution of 12.4 g 4-methylthiophenol and 10.7 g 2,6-lutidine in 50 mL acetone was treated with 18.4 g cyanuric chloride in 200 mL acetone, to give 1.16 g 2,4-dichloro-6-(4-methylphenylthio)-1,3,5-triazine (II). II (1840 ppm) very markedly decreased transpiration rate and increased leaf diffusion resistance, in potted bean (Phaseolus vulgaris). In isolated pea chloroplasts, 2,4-dichloro-6-(2,6-dichlorophenoxy)-1,3,5-triazine (622 g/L) had no effect on photosynthetic electron transport, as shown by absence of O uptake inhibition. This was contrasted to 65% O uptake inhibition caused by the standard atrazine (108 g/L).

IT **112720-19-1P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of, as plant antitranspirant)

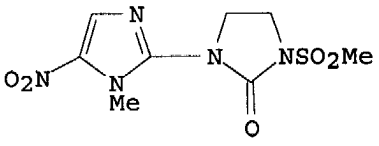
RN 112720-19-1 HCAPLUS

CN Quinazoline, 4-[(4,6-dichloro-1,3,5-triazin-2-yl)oxy]- (9CI) (CA INDEX

NAME)



L40 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:603875 HCAPLUS
DOCUMENT NUMBER: 101:203875
TITLE: Nitroimidazoles: part XIX - structure-activity relationships
AUTHOR(S): Nagarajan, K.; Arya, V. P.; George, T.; Nair, M. D.; Sudarsanam, V.; Ray, D. K.; Shrivastava, V. B.
CORPORATE SOURCE: Res. Cent., CIBA-GEIGY, Bombay, 400 063, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1984), 23B(4), 342-62
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

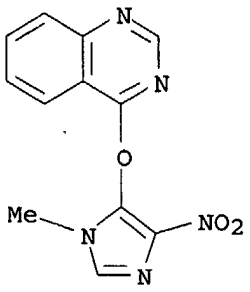


I

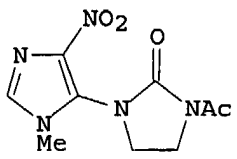
AB A variety of nitroimidazoles, mostly 1,2-disubstituted-5-nitro derivs. were examined for in vitro activity against Entamoeba histolytica and for effectiveness in treating early hepatic infection in golden hamsters. Many compds. carried a functionalized N atom at position 2. In vivo activity was observed with 1-alkyl-5-nitroimidazoles carrying a substituted imidazolidinone or imidazole. Among these derivs., 1-methylsulfonyl-3-(1-methyl-5-nitro-2-imidazolyl)-2-imidazolidinone (I) [56302-13-7] was the most potent against hepatic and caecal infections of E. histolytica in the golden hamster and Trichomonas foetus infections in mice. It was developed as a drug for treatment of amoebiasis, giardiasis, and trichomoniasis. The structure-antiamebic activity relationships of the nitroimidazoles are discussed.

IT **86231-03-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amebicidal activity of, structure in relation to)

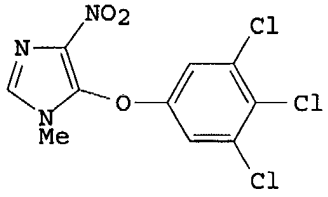
RN 86231-03-0 HCAPLUS
CN Quinazoline, 4-[(1-methyl-4-nitro-1H-imidazol-5-yl)oxy]- (9CI) (CA INDEX NAME)



L40 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:422379 HCAPLUS
DOCUMENT NUMBER: 99:22379
TITLE: Nitroimidazoles. Part XVI. Some 1-methyl-4-nitro-5-substituted imidazoles
AUTHOR(S): Arya, V. P.; Nagarajan, K.; Shenoy, S. J.
CORPORATE SOURCE: Ciba-Geigy Res. Cent., Bombay, 400 063, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1982), 21B(12), 1115-17
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 99:22379
GI

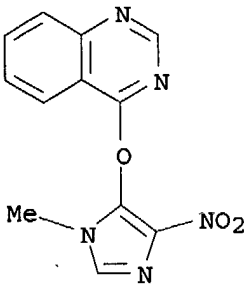


II



III

AB Treatment of 1-methyl-4-nitro-5-chloroimidazole I with 5-membered lactams, e.g. imidazolidinones, oxazolidinone, and thiazolidinone, and imidazole affords N-imidazolyl derivs., e.g. II. Amino derivs. are similarly obtained. 2-Hydroxypyrazine, 4-hydroxyquinazoline, and 3,4,5-trichlorophenol and I react to form O-derivs., e.g. III, while mercaptans provide the sulfides.
IT **86231-03-0P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 86231-03-0 HCAPLUS
CN Quinazoline, 4-[(1-methyl-4-nitro-1H-imidazol-5-yl)oxy]- (9CI) (CA INDEX NAME)

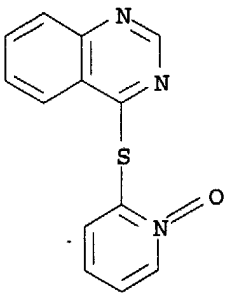


L40 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:582339 HCAPLUS
DOCUMENT NUMBER: 97:182339
TITLE: Quinazolines, their preparation and biological activity
AUTHOR(S): Schoenowsky, Hubert; Sachse, Burkhardt
CORPORATE SOURCE: Pflanzenschutzforsch.-Chem., Hoechst A.-G., Frankfurt/Main, D-6230/80, Fed. Rep. Ger.
SOURCE: Zeitschrift fuer Naturforschung, Teil B: Anorganische Chemie, Organische Chemie (1982), 37B(7), 907-11
CODEN: ZNBAD2; ISSN: 0340-5087
DOCUMENT TYPE: Journal
LANGUAGE: German

AB 4-Hydroxyquinazolines (I) were prepared by cyclocondensation of 2-aminobenzoic acids with formamide and were alkylated and arylated to give alkoxy- and (aryloxy)quinazolines. 4-Chloroquinazolines were prepared by treatment of I with PCl5/POCl3 and were converted into thio and amino compds. by reaction with mercaptans and amines, resp. A number of the quinazolines showed fungicidal activity.

IT **83529-97-9P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)

RN 83529-97-9 HCAPLUS
CN Quinazoline, 4-[(1-oxido-2-pyridinyl)thio]- (9CI) (CA INDEX NAME)



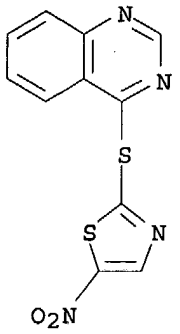
L40 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:4286 HCAPLUS
DOCUMENT NUMBER: 78:4286
TITLE: 5-Nitro-2-thiazolyl sulfides
INVENTOR(S): Hughes, Peter Graham; Verge, John Pomfret
PATENT ASSIGNEE(S): Lilly Industries Ltd.

SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2213558	A	19721005	DE 1972-2213558	19720321
GB 1354296	A	19740522	GB 1971-8252	19710330
US 3870725	A	19750311	US 1972-234376	19720313
CH 545812	A	19740215	CH 1972-4021	19720316
IT 965768	A	19740211	IT 1972-49259	19720327
FR 2132133	A5	19721117	FR 1972-10848	19720328
FR 2132133	B1	19750620		

PRIORITY APPLN. INFO.: GB 1971-8252 A 19710330
GB 1971-39106 A 19710820

GI For diagram(s), see printed CA Issue.
AB Forty-five title compds. (I, R = substituted 1.3,4-thiadiazol-k-yl, 5-thioxo-1.3,4-chiadiazol-2-yl, 1.3,4-oxadiazol-k-yl, 1.2,4-triazol-1(or 5)-yl, 1.2,3,4-tetrazol-5-yl, 1.2,4-triazin-1-yl, 4-quinazolinyl, 2-pyrimidinyl, 2(or 4)-pyridyl, or 2-quinolyl), useful as fungicides, were prepared by reaction of the bromo derivative II with RSX (X = H, K, Na).
IT **40045-66-7P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 40045-66-7 HCAPLUS
CN Quinazoline, 4-[(5-nitro-2-thiazolyl)thio]- (9CI) (CA INDEX NAME)

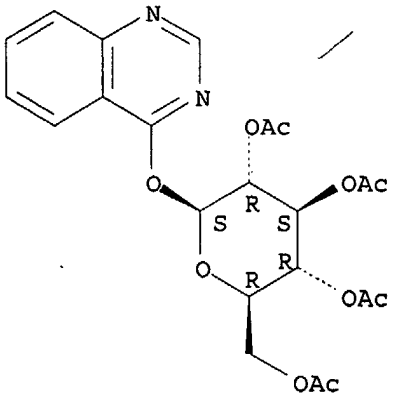


L40 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:413319 HCAPLUS
DOCUMENT NUMBER: 71:13319
TITLE: Glycosides and heterocycles. XXXV. Glycosides of hydroxy- and mercaptoquinazolines
AUTHOR(S): Wagner, Guenther; Suess, F.
CORPORATE SOURCE: Pharm, Inst., Karl-Marx-Univ., Leipzig, Fed. Rep. Ger.
SOURCE: Pharmazie (1969), 24(1), 35-8
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB 4-Hydroxyquinazoline (I) Ag salt (7.59 g.) was mixed with 300 ml. C6H6,

250 ml. solvent was distilled, a solution of 4.11 g. tetra-O-acetyl-α-D-glucopyranosyl bromide (II) added, the mixture refluxed 2 hrs. and filtered, the filtrate evaporated, and the residue purified by thin-layer chromatog. on SiO2 in the solvent system 3:2 AcOEt-cyclohexane to yield 40% 4-(tetra-O-acetyl-β-D-glucopyranosyloxy)quinazoline (III) (Q = tetra-O-acetyl-β-D-glucopyranosyl throughout this abstract), m. 150-2° (MeOH), [α]20D -22.5° (c 2.5, CHCl3). I Hg salt (1.62 g.) and 2.71 g. II refluxed for 2 hrs. in 100 ml. MePh and filtered, the filtrate washed with Na2S2O3 and 5% NaOH and evaporated gave, after addition of MeOH, 50% 3-(tetra-O-acetyl-β-D-glucopyranoysl)-4-quinazolinone (IVa), m. 192-4° (70% MeOH), [α]20D 0° (CHCl3). III (0.52 g.) and 2.02 g. HgBr2 refluxed 2 hrs. in 50 ml. anhydrous PhMe afforded 80% IVa. IVa deacetylated by heating in 0.05M MeONa gave 70% 3-β-D-glucopyranosyl-4-quinazolinone (IVb) (G = β-D-glucopyranosyl throughout this abstract), m. 257.5-8.5° (PrOH), [α]20D 37.3° (c 2.3, HCONMe2). A solution of 1.82 g. 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranose and 0.82 g. 4-chloroquinazoline in 16 ml. Me2CO was treated with 0.28 g. KOH in 4 ml. H2O, agitated 25 min., and diluted with 100 ml. H2O to yield 84% 4-(tetra-O-acetyl-β-D-glucopyranosylthio)quinazoline (Va), m. 95-6° (MeOH), [α]20D 12° (c 3, CHCl3). 2-Chloroquinazoline gave similarly 40% 2-(tetra-O-acetyl-β-D-glucopyranosylthio)quinazoline (VIa), m. 143-5° (30% MeOH), [α]20D 13° (c 3, CHCl3). A mixture of 0.5 g. IVa and 1.2 g. P4S10 in 5 ml. anhydrous C5H5N heated 5 hrs. at 130° and 10 hrs. at 160°, cooled, extracted repeatedly with CHCl3, the combined exts. washed with 5% NaOH, evaporated, and the residue treated with MeOH, gave 70% 3-(tetra-O-acetyl-β-D-glucopyranosyl)-4-quinazolinethione (VII), m. 174.5-5.5° (50% MeOH), [α]20D 7° (c 2.2, CHCl3). The reaction of 4-quinazolinethiol and II in aqueous Me2CO in the presence of NaOH yielded 56% Va and 8% VII. Deacetylation of Va with MeOH gave 85% 3-β-D-glucopyranosyl-4-quinazolinethione (Vb), m. 218-20° (PrOH), [α]20D -19° (c 3.4, HCONMe2). The reaction of 2-hydroxyquinazoline and II in aqueous Me2CO in the presence of NaOH followed by preparative thin-layer chromatog. on SiO2 in 3:2 C6H6-EtOAc gave 5% 2-(tetra-O-acetyl-β-D-glucopyranosyloxy)quinazoline, m. 119-21° (35% MeOH), [α]20D 8° (c 2.5, CHCl3). 2-Quinazolinethiol reacted with II in aqueous Me2CO afforded 38% VIa. Deacetylation of VIa with MeONa gave 60% 2-(β-D-glucopyranosylthio)quinazoline (VIb), m. 113-15° (PrOH), [α]20D. -96.4° (c 2, HCONMe2). Uv spectrum of IVa was very similar to that of 3-methyl-4-quinazoline and differed from the spectrum of 1-methyl-4-quinazoline. This confirmed the structure of IVa.

IT **24558-70-1P 24577-13-7P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 24558-70-1 HCAPLUS
CN Quinazoline, 4-(β-D-glucopyranosyloxy)-, 2',3',4',6'-tetraacetate (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 24577-13-7 HCAPLUS
CN Quinazoline, 4-(β-D-glucopyranosylthio)-, 2',3',4',6'-tetraacetate (8CI) (CA INDEX NAME)

Absolute stereochemistry.